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THE CHANGING PATTERN OF DISEASE IN CHILDHOOD

THE BLACKADER LECTURE

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MAY I BEGIN by saying how deeply conscious I am of the honour conferred on me by the invitation from the Canadian Medical Association to give the Blackader Lecture for 1955.

Dr. Blackader, the father of Canadian pædiatrics, graced and adorned his profession for many years. Not only did he make valuable contributions to his chosen branch of medicine, but he also had a long and distinguished career in medical journalism, culminating in 1921 in the editorship of the *Canadian Medical Association Journal*. By his far-reaching vision and his ready pen he succeeded, in a remarkably short space of time, in making the Journal representative of medicine throughout the Dominion and securing for it a reputation as one of the world's important national medical publications.

In choosing a subject on which to address you I have been conscious of the fact that those who have preceded me in giving this Lecture have avoided clinical dissertations on disease and have drawn on their experience of pædiatrics in more general terms. It is therefore with this in mind that I have chosen as the title of my Lecture "The Changing Pattern of Disease in Childhood".

My remarks concern pædiatric practice as I have seen it in Glasgow—a large industrial centre, the hub of the iron, steel and shipbuilding industries in Scotland, and subject to those fluctuations in prosperity and employment which characterize industrial centres all over the world. Although magnified in some respects because of the large population served, I imagine the nature and incidence of disease differ little from those seen in comparable areas of Britain or in Canada.

It can be considered a truism to say that the last 25 years have witnessed a revolution in pædiatric practice. The improvement in the morbidity and mortality rates has exceeded the most optimistic estimates. I have been impressed, as have many others, by the difference in the nature and type of disease which we now see as compared with those in the years following the First World War. The change has of course been a gradual one—the disappearance of certain diseases, the diminution in the incidence of others and the appearance, or perhaps I should say the recognition, of many that are new.

Of all these changes none is more striking than the fall in the incidence and the mortality of the infectious diseases and of infections generally. Diphtheria, for example, is now so rare that it is no longer to be seen by the undergraduate student, and I would like to pay tribute to the work of those Canadians who were the leaders in the prevention of this disease. Scarlet fever too has diminished not only in incidence but also in severity. The toxic type (malignant scarlet fever) is now not seen, and indeed the body's reaction to the hæmolytic streptococcus varies so widely that scarlet fever is no longer regarded as a specific infectious disease but merely as one of the varied responses to a streptococcal infection. As a sequel to this diminution in the incidence of hæmolytic streptococcal infections there has been a parallel fall in juvenile rheumatism, but for some strange reason not in acute nephritis.

For this partial ascendancy in the control of infections, the sulphonamides and the antibiotics must be given the credit which is their due, but there is considerable statistical evidence that many diseases such as scarlet fever and rheumatism were diminishing in incidence and severity

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even before 1935 when the sulphonamides were introduced. Similarly, the Registrar-General's Reports show that deaths from infantile diarrhœa which contributed materially to the mortality rate in infants until the late thirties fell sharply after 1915—and have, in fact, continued to fall until the present time (Table I).

TABLE I.

DEATHS FROM DIARRHŒAL DISEASES IN THE FIRST YEAR OF LIFE

	Deaths per 1,000 births			*Deaths per 1,000 births*	
	England and Wales	*Scotland*		*England and Wales*	*Scotland*
1901-05....	——	14.9	1936-40....	4.95	8.1
1906-10....	——	13.1	1941-45....	4.92	8.7
1911-15....	19.24	13.3	1946-50....	3.29	6.0
1916-20....	9.34	9.4	1951.....	1.22	2.4
1921-25....	8.14	7.3	1952.....	1.01	1.7
1926-30....	6.47	6.3	1953.....	0.97	1.5
1931-35....	5.65	7.2			

There are probably many causes for this fall in mortality from infections. In the first place there is no doubt that the interest shown in diseases of children has increased in recent years. In many medical schools, organized and compulsory teaching of pædiatrics as a special branch of medicine is not much more than 25 years old. The improvements in the social services, however, have probably played an even greater part. There is better nursing, better health education, improved hygiene in the home, smaller families and, above all, a greater sense of social responsibility. The large families of the Victorian days with the attendant poverty and often ignorance are seldom encountered today.

In nutrition also great advances have been made. The discovery of vitamins in 1912 by Gowland Hopkins in Great Britain and by Casimir Funk in the United States and the large volume of research work since then have resulted in a disappearance of deficiency diseases, especially rickets, from the infant population. We have been taught to recognize the frequency of iron-deficiency anæmia and, while not fully understanding the mechanism of iron metabolism, can treat it successfully. Infant feeding will be discussed later; suffice it to say here that the marasmic infant whose presence in the ward was a challenge to those responsible for his care has now almost disappeared.

The administration of parenteral fluid has passed through various stages, from the subcutaneous and intraperitoneal routes to the intravenous. Blood or one of the various electrolyte solutions can now be safely and easily given to the smallest infant if desired. Our knowledge of the behaviour of water and electrolytes has grown steadily and has probably contributed as much as any other single factor to the cure of infant ailments and the saving of life.

In neonatal diseases the recognition and treatment of Rhesus incompatibility, the enlightened care of premature infants and the recognition of the ill-effects of anoxia are all important landmarks in progress during the last three decades. Even in the field of congenital abnormalities, recognition of certain causes, such as virus infection in the early months of pregnancy, and the effect of certain noxious substances has led to hopeful forms of prevention.

It must be admitted, however, that in solving the old problems we have created new and perhaps more difficult ones. One such example of a new problem which comes to mind is the appearance within recent years of retrolental fibroplasia resulting from the prolonged and excessive use of oxygen in the treatment of very small premature infants. As more of these small infants survived with oxygen therapy, so did the increased incidence of retrolental fibroplasia become apparent. The condition, which is characterized in the early stages by dilatation and tortuosity of the retinal vessels, progresses to the formation of an opaque and retrolental fibrous mass and permanent blindness. While it is true that oxygen therapy may be life-saving for the infant, the work of Ashton and others has shown quite clearly that administration of oxygen in concentrations of over 40%, especially if prolonged, results in a percentage of the treated infants being affected. On the other hand, if an infant is not exposed to high concentrations and if the duration of therapy is not unduly long, it is unlikely that retrolental fibroplasia will occur. At the Glasgow Maternity Hospital with over 3,500 births a year, four cases were seen in 2½ years. These were all under 4 lb. in weight at birth. No case has been seen since June 1953 when the policy of restricted oxygen therapy was introduced. It would appear therefore that the problem arising directly from the use of oxygen therapy in very small infants has been quickly solved.

Again the increased use of BCG to protect newborn infants against tuberculosis has made

the tuberculin tests valueless as a diagnostic criterion of tuberculous infections in early infancy and childhood, and the diagnosis of primary tuberculosis must now rest on the clinical and radiological manifestations alone.

Many such examples as these could be given and one could draw attention to the appearance of new clinical pictures in certain diseases such as chronic tuberculous meningitis brought about by modern anti-tuberculosis treatment or to the later stages of the nephrotic syndrome which, because of the prevention of infection, progresses to hypertension.

In addition to changes in the pattern of disease arising from survival or prolongation of life in conditions formerly fatal, one must also take account of newly recognized diseases such as fibrocystic disease of the pancreas, hiatal hernia and that fascinating group of metabolic disturbances associated with amino-aciduria and renal tubular defects such as the Fanconi syndrome, hyperchloræmic acidosis and perhaps idiopathic hypercalcæmia.

We must all realize that our success in treating disease has thrown into prominence certain social and psychological problems which have for so long been neglected or ignored by the medical profession.

This then in broad outline is the changing picture of pædiatrics as it has been unfolded during the past three or four decades. I should like in the remaining time at my disposal to make some observations on three important pædiatric problems—infant mortality and morbidity, infant feeding and diarrhœal diseases and, thirdly, rickets and convulsions.

INFANT MORTALITY AND MORBIDITY

As long ago as 1910 Sir Arthur Newsholme[10] stated that the infant mortality was "the most sensitive index we possess of social welfare and of sanitary administration". This has been accepted up to the present time and broadly speaking is still true, but as the infant mortality has fallen to such low levels in western countries it may be necessary, if one must have an index, to substitute morbidity for mortality.

It may be helpful to review broadly the course of infant mortality in England and Wales since the introduction of universal registration of deaths in 1837. In 1850 the infant mortality rate was 153 and with slight variations in the intervening years remained in 1900 unchanged at 153. In the next 50 years the rate fell to 28 in 1950, and in 1954 the provisional rate was 27. The figures for Scotland are slightly higher and for this there are several reasons. This great fall in infant mortality which, in a city such as Glasgow with approximately 20,000 births a year would result in a saving of some 2,400 infant lives each year, was brought about mainly by a fall in the death rate from the end of the first month to the end of the first year. This postnatal period is the one during which infection takes its greatest toll, and it is by the prevention and cure of these infections that most of the reduction has been brought about.

The neonatal mortality on the other hand remained relatively unchanged during the first part of the century and has shown improvement only during the last two decades. At the turn of the century it was over 40 and by 1930 had fallen only to 38: it is now 18 and comprises no less than 65% of the total infant mortality. This "hard core" of neonatal deaths results from such conditions as asphyxia, congenital abnormalities, intracranial hæmorrhage and the like, with prematurity a strong predisposing factor. One cannot expect the infant mortality to fall much lower unless these diseases can be favourably influenced or the incidence of prematurity reduced.

Thus it appears that the relative importance and significance of the two components of the infant mortality have undergone a change. Furthermore it has been suggested that a clear picture of the total loss of life would be obtained only by including the stillbirths with the neonatal deaths to give a figure for a perinatal mortality. It is, as everyone knows, fortuitous whether a very small premature infant shows signs of life and is classed as a liveborn infant or shows no signs of life at birth and is classed as stillborn. A perinatal mortality rate compiled in this way would give a true assessment of the loss of life at birth while the postnatal mortality —that is, deaths from the end of the first month, the only other component one need consider— would comprise the deaths resulting mainly from infection. With the means available for overcoming and preventing most of the infections, this postnatal mortality might well assume the significance as an index of social welfare which Newsholme attached to the infantile mortality some 45 years ago.

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In several countries, however, the postnatal mortality rate is below 10 per 1,000 births, and to get an even more sensitive index one must take account of the morbidity in this period. It should be recalled that this was suggested by Farr about the middle of the last century. Farr, whose great contribution to the study of infant mortality and child welfare is recognized by all, considered the establishment of a register of sickness as "an invaluable contribution to therapeutics as well as to hygiene". At that time such a register was kept on a small scale in some English towns but was soon abandoned. In the present day the notification of certain infectious diseases can be regarded as accomplishing this object in a small way. In some areas in Great Britain, pneumonia is a notifiable disease and in other centres, juvenile rheumatism. This was primarily to facilitate the study of the life history of these diseases and their distribution in the population, but such a procedure could be extended to include at least the common diseases in the age period under discussion. Suggestions have been made that there should be some better means of recording and tabulating the morbidity in the first year of life to give a true picture of the health of the infant in a particular community.

Dykes[5] has attempted this in Luton. In a study of morbidity and mortality in infants, he found that although the mortality rates in infants of the well-to-do were lower than those of the lower-income groups, the sickly infant was as common in one as in the other. Where they differed was in the fact that the infant in the poorer classes was more likely to die. Dykes concluded that no substantial reduction in sickness could be expected from such general measures as fall within the scope of public health and social medicine. Douglas[4] was unable to confirm these findings, and in a survey drawn from infants of all social classes and from all parts of Great Britain he found social class differences both in mortality and morbidity during the first year of life.

Titmuss has also discussed the implications of the social scale in infant mortality and has stated that infants of the poorer classes are *relatively* worse off today than before the First World War. The well-to-do have benefited more by the advances in modern medicine than the others, although one might have expected the reverse to be true. It would have seemed reasonable to think that the improvement in social services during the past 30 years would have caused a greater fall in the mortality of the lower-income classes than in the well-to-do. It must be assumed therefore that if the constitution of the poorer-class infants is not worse, the influences to which they are subjected after birth must be. Douglas[4] points out that if all the social classes had the same infant mortality rate as the well-to-do, there would be a saving in the United Kingdom of about 10,000 lives during the first year of life.

Although the steep fall in the infant mortality during the last 25 years tends to cause complacency, such considerations as the above point the way to still further improvement.

INFANT FEEDING AND INFANTILE DIARRHŒA

It is probably true that infant feeding, by which I mean the practice of formulating rules as to what and how much an infant should be fed, has ceased to be a problem. Until about 100 years ago most infants were fed at the breast; if they were not, their chances of survival were poor. More recently, in this century, the bottle-fed infant having suffered from repeated infections provided a common clinical problem. Feeding at the breast has steadily declined, especially during the last 25 years, until today its virtues and advantages are being questioned even in authoritative textbooks. The wet-nurse of the fashionable early Victorian period is no longer acceptable.

The increase in the number of artificially fed infants hastened the investigations as to how best to use cow's milk. The literature from 1900 until the mid-twenties abounds with articles extolling the advantages and disadvantages of percentage-feeding and attempting to explain why an excess of fat or carbohydrate in the diet might cause diarrhœa. Certain virtues were attached to the various sugars and instructions laid down for their use. Indeed, lactose, the sugar occurring naturally in milk, was said to have the disadvantage that it was not absorbed and digested as well as other sugars (Marriott[8]). Combinations of various sugars depending on whether the infant tended towards constipation or diarrhœa were popular.

These so-called scientific methods of infant feeding with rigid formulæ and the "alarm-

clock" regimen stemmed mainly from Germany, but were taken up enthusiastically in other countries. By the critical experiment of feeding two groups of infants, one on cow's milk protein and breast milk whey and the other on breast milk protein and cow's milk whey, Finkelstein concluded that the former containing the high protein and low salt content was the better and therefore to be used in all kinds of digestive upsets. As a direct result of these observations he recommended the use of "Eiweissmilch" (protein milk) and for many years it was used throughout most countries of the western world in the treatment of diarrhœa. Diarrhœa was at that time treated entirely by dietetic measures, which seemed to lead to the reasonable assumption that dietary defects were the cause. Such terms as fermentative diarrhœa, fat dyspepsia and alimentary toxicosis were used from time to time.

There was in Great Britain, however, a healthy scepticism about the dietary origin of diarrhœa in the infant. The advances in bacteriology at the turn of the century had shown that in some epidemics dysentery and enteric fever were mainly concerned. There were, however, fearful outbreaks of diarrhœa (cholera infantum) occurring each summer and worse in the hot, dry weather than when it was cold and wet, which had the hallmark of infection rather than a dietetic error, and breast-fed infants were relatively unaffected.

Thus gradually, nutritional factors as the cause of diarrhœa in infancy were given up to be replaced by infection. All diarrhœa in infants is basically due to infection, and in retrospect it seems strange that the recognition of the infectivity of infantile diarrhœa in hospital wards was so long delayed. The fact that the organism causing the infection could not be determined was probably an important factor in delaying this recognition and is perhaps the only really valid one. The causal organism is still unknown. In 1945 Bray,[3] and in 1948 Giles and Sangster,[6] isolated a special type of *Bacterium coli* from the fæces of infants with diarrhœa and demonstrated the presence of antibodies in the serum. Much investigation has been carried out along these lines and similar reports have come from France, Germany and the Scandinavian countries and America. The terminology was at first confused and these organisms were variously designated as D433, alpha and beta strains and so on. They are now referred to by their somatic antigens, the most important being 0111 and 055. Increasing numbers of coliform strains such as 026 have also been incriminated though they are relatively uncommon. We have found these special types of *Bacterium coli* in about one-third of all cases of diarrhœa admitted to the wards (Shanks and Studzinski[14]) but whether they are the *causa causans* or not still remains a moot point.

It is worth while recalling that in 1909 Morgan and Ledingham[9] recovered a special bacillus called Morgan's bacillus from a large percentage of the stools in summer diarrhœa and believed it to be related causally to the diarrhœa. However, Morgan's bacillus is not infrequently found in the normal stools of healthy infants and adults; and so are the special types recognized since 1945. Stevenson[15] found the 0111 strain (D433) present in the stools of one in 200 of the adult hospital patients in the Glasgow area.

It is at least reasonable to suggest that these Gram-negative bacilli of special types are secondary invaders which appear from time to time and vary with the years, and that the true cause of gastro-enteritis still eludes us. Although in American literature the evidence would seem to favour a virus infection (Light and Hodes[7]), one is drawn to the conclusion that infantile diarrhœa is an infection the true cause of which is not yet known. It is highly probable that it is not a single entity but owns many causes.

RICKETS AND CONVULSIONS

Although rickets has been a disappearing disease for over 30 years, the history of this disease and the unfolding of the varying factors concerned in its etiology form one of the most fascinating chapters in the whole of medicine. So many fundamental principles of human nutrition and clinical medicine are embraced in its understanding that it might almost be said to occupy the place in the teaching of pædiatrics that typhoid fever occupied in the teaching of general medicine in Osler's day. Leonard Findlay's experimental work in 1908 did much to stimulate interest in the etiology of this disease which with the rise and spread of slums in the industrial areas during the Victorian period had become one of the chief causes of crippling and

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disease in the early years of life and of serious deformities in the adult. It was, however, the discovery of the accessory food factors which furnished the real clue to the solution of the problem.

In most western countries infantile rickets as a deficiency disease and in its florid form is now a medical curiosity, and since the war its existence even in a mild form is rare. It still has, however, to be reckoned with as a complication of other morbid processes such as cœliac disease, renal failure and those lesions involving the renal tubules such as the Fanconi syndrome. The fascinating work of Jonxis and others who have recently demonstrated the presence of aminoaciduria in infantile rickets serves to remind us that our knowledge of the mysteries of this disease is still incomplete. We have as yet very little knowledge of the actual mode of action of vitamin D, although admitting that it will in the course of a few days increase the retention of calcium and phosphorus tenfold.

Throughout the industrial era Glasgow had an unenviable reputation for the prevalence of rickets, which may or may not have been justified: if it was, it was merely a reflection of the industrial nature of the community and the inadequacy of the housing of the masses of workers at the turn of the century. Housing was then, and still is, inadequate. Glasgow tenements, usually four storeys high with narrow streets between, favoured the development of rickets, and the argument of Leonard Findlay that lack of exercise was a primary etiological factor was based on his clinical experience in a community housed in such tenements. In the decade from 1920 onwards rickets was still frequently seen in the wards of the hospital. The cod-liver oil and phosphorus era had just ended to be replaced by cod-liver oil alone tested for its antirachitic activity and there soon appeared a host of proprietary preparations all of which were efficient in promoting the retention of calcium and phosphorus. Cod-liver oil was first distributed free by the Government in 1919, and by 1930-40 rickets had already disappeared, although a mild form persisted into the middle of the next decade.

In 1943 the British Pædiatric Association conducted an extensive investigation into the occurrence of rickets during wartime.[4] This was suggested because the impression had been formed that in certain parts of the country there had been an increase in its incidence during the war years. Of 4,818 children from 3-18 months of age taken from all parts of the British Isles, 12½% were said to have some clinical evidence of rickets. There was, however, poor agreement between the clinical evidence and the radiological evidence, and in the first year of life the incidence by x-ray findings was only 4%. These figures can be taken to indicate that the number of infants suffering from frank rickets was small and that in assessing accurately the presence or absence of rickets in its mild form, examination of the blood would be necessary.

In 1942, one year earlier, we had carried out a special investigation into the incidence of craniotabes in 972 infants under one year of age admitted to the Royal Hospital for Sick Children, Glasgow, during the year beginning October 1, 1941. Generalized skull softening and suture softening were not included. No less than 26% of these showed craniotabes. The highest incidence was in the first six months and none was found after the tenth month. The seasonal incidence conformed to that of frank infantile rickets—a peak in March and the lowest incidence in July. Blood examination of 118 of the affected infants showed 61 to have biochemical evidence of rickets (approximately 50%). Thus, if one-quarter of the infants studied showed craniotabes and one-half of these had biochemical evidence of rickets, the incidence of craniotabes which could be ascribed to rickets was about 12.5%.

At that time, because of the shortage of milk due to the war economy, the Government arranged to supply a subsidized dried milk (National Dried Milk) for the artificial feeding of infants. This milk had added to it vitamin D so that the reconstituted milk contained 700 international units per pint: this preparation rapidly gained favour and is now extensively used. The effect of this measure on the incidence of craniotabes was striking. Since about 1943, craniotabes unless in very small and rapidly growing premature infants has been seldom seen even in the late winter and spring months and in large industrial centres such as Glasgow. All infants fed on National Dried Milk (and in Glasgow this amounts to at least 90% of artificially fed infants) get approximately 1,000 i.u. of vitamin D from the milk daily, and many in addi-

tion are given cod-liver oil or one of the proprietary preparations, often in generous doses.

There is no doubt therefore that many infants are in fact getting more vitamin D than is required for the prevention of rickets and it is now being suggested that idiopathic hypercalcæmia might result from this overdosage. Whether hypercalcæmia is a new clinical entity or only now being recognized is a debatable point. Certainly serum calcium estimations have been made in large numbers from about 1920 onwards, and until recently high calcium values were not found except in exceptional and understandable cases where massive vitamin D dosage was continued for an unduly long period. It may be that some infants are sensitive to vitamin D just as certain infants are resistant (vitamin D resistant rickets). I have, however, found hypercalcæmia in an infant who has never been fed on dried milk and who, as far as can be ascertained, has never had any vitamin D, except the small amount contained in sterilized cow's milk. The infant was, however, breast fed for the first three months, during which time the mother was taking cod-liver oil. He then developed anorexia and constipation, failed to gain weight and was weaned on to liquid cow's milk. At 4½ months when first seen at hospital, his serum calcium was 14.5 mg. per 100 ml. Vitamin D preparations were withheld and his calcium intake was reduced as a temporary measure; in two months his blood calcium had returned to normal and he has since thriven well.

The etiology of idiopathic hypercalcæmia is therefore still *sub judice*. Meanwhile the omission of all vitamin D supplements from the diet is indicated. The use of low calcium milks has been suggested and is worthy of a clinical trial. Theoretically, however, it is the calcium retained within the body and not the dietary intake which is of significance, and the retention of calcium is regulated mainly by vitamin D. It has recently been stated (Anderson *et al.*[1]) that cortisone may be antagonistic to vitamin D, and further observations on this are urgently required.

Convulsions: Coincident with the fall in the incidence of rickets there has been a change in the etiological pattern of convulsions in infancy. In the years following the First World War and up to 1940, the admission of infants with convulsions to the Royal Hospital for Sick Children, Glasgow, showed a distinct seasonal variation which followed the seasonal curve of rickets. Blood examination showed that many of these infants had hypocalcæmia and were in fact suffering from tetany. This hypocalcæmic nature of infantile convulsions was generally accepted. For example, Powers[12] showed that the convulsions which frequently complicate whooping-cough in infancy were often hypocalcæmic. This, I understand, is no longer so.

Shanks[13] has studied the incidence of convulsions in three representative quinquennia, 1922-26, 1932-36 and 1942-46. The findings were interesting in so far as the seasonal curves were those characteristic of frank tetany in the first two periods but not in the third. The most important fact which emerged, however, was not the probable disappearance of hypocalcæmia as suggested by the altered seasonal incidence, but the fact that the total and relative incidence of convulsions remained unaltered in the three periods.

In 1922-26 convulsions formed 7.9% of the admissions and in 1942-46 again 7.9%. The policy of admissions to hospital had not been altered during these years. The serum calcium of 64 infants admitted with convulsions during a 12-month period in 1947-48 was estimated; in only two was hypocalcæmia found and one of these was suffering from manifest tetany.

It may of course be argued that the ionic blood calcium is reduced although the total calcium remains normal. This was not the case in the first two quinquennia, nor were any disturbances of acid-base balance apparent in any of the 64 infants whose blood was examined. These facts have not been adequately explained and further observations are obviously called for. To postulate an inherent tendency to convulsions in some infants, even if true, would be no solution. It would seem that, whatever the true cause may be, the hypocalcæmia which was seen so frequently until 1940 and which has now disappeared was merely the precipitating factor.

Peterman, whose contributions to the literature of convulsions have extended over a long period, has emphasized the importance of recognizing the seriousness of febrile convulsions in infancy, many of which were in the past associated with hypocalcæmia. If fever *per se* produces an alkalosis, one might suggest that the alkalosis results in a fall in the free calcium of the blood although the total calcium content remains un-

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altered. The free calcium content of the blood, however, cannot be easily estimated except by an indirect method, and as far as I know the evidence in favour of this hypothesis is not convincing. One might conclude these comments on convulsions by quoting Peterman's statement[11] that in the majority of children suffering from convulsions the electroencephalogram shows signs of an organic cerebral lesion with cerebral dysrhythmia of the petit mal or grand mal type.

Thus, over the past 30 years the incidence of convulsions remains unaltered in the hospital population, but the precipitating factor of hypocalcæmia has disappeared.

GROWTH OF SOCIAL PÆDIATRICS

It will be helpful to discuss briefly where the advances in etiology and treatment of disease are leading us. The success achieved in the cure and prevention of disease has thrown into prominence the problems of social and psychological medicine. Trevelyan defined social history as history without the politics: social medicine may be defined as medicine without the treatment of disease. Attention must be directed more to the child and his illness as it is seen against the background of his family and the community in which he lives.

In Great Britain the industrial revolution reached its climax in the last quarter of the nineteenth century and brought with it the problem of poverty and neglect. It is only within recent years that the impact of these social evils on society in general and on child health in particular has been fully appreciated. The present-day attitude is indicated by the fact that in Great Britain the university chairs which pædiatricians hold are without exception, as far as I know, Chairs of Child Health, or have these words as part of their title.

The futility of a period in hospital for many small children, even allowing for the benefits of modern treatment, is only too apparent when we see the results of a return to the environment which was responsible for the patient's illness in the first place. The sick or ailing mother living in poor conditions with a child suffering from a chronic upper respiratory tract infection and basal lung lesions can be cited as an example. In hospital the infection can be reasonably well cleared up and the lung lesions regress, but on return to the poor environment the condition recurs within a few weeks or months.

Thus there is great need for each one of us to enquire into the reason for the child's admission to hospital. A rough analysis will often show that about one-third of the medical patients are admitted for socio-economic reasons—illness of the mother, inadequate housing conditions, ignorance or undue anxiety of the parents and so forth.

In addition to this, consideration must be given to the added stress and strain under which children are brought up today. Many social workers and pædiatricians are perturbed by the increasing amount of emotional ill-health and the associated disturbance of family relationships which are so apt later on to result in juvenile delinquency and neurosis of various kinds.

Psychology like all new sciences is much influenced by waves of thought dominating a particular period of time, and extremes must be avoided. Great importance is laid on the separation of the child from his mother during his early formative years. Child psychiatrists working in child guidance clinics estimate that in 80% of cases the genesis of the psychological disorder lies in the first seven years of life and that separation of mother and child during these years may cause profound emotional disturbances. This has been shown to be so by a number of investigators (Bowlby[2]) and we must accept it.

The problem is a very complex one. The infant and small child should be considered in relation to his family, which is the unit of society in the community. Failure to realize this and replace it by a purely scientific approach is not in the child's best interests. In the early years of the present century pædiatrics was inclined to be too scientific, too business-like, but excessive mother love often mixed with anxiety and apprehension and the protection of the child from all emotional disturbances is surely an over-correction. Parents are obliged to steer a middle course between the Scylla of demonstrative affection which spoils the child and the Charybdis of spartan treatment which characterized the upbringing of the child in the Victorian age.

In any scheme of child care therefore, whether social or having to do with mental health, the family doctor rather than the hospital physician has the vital role to play. He subconsciously sees the child in relation to the other members of the

family, to everybody's advantage. The consideration of human relationships has always been part of his daily work and he, not the pædiatrician or the child psychiatrist, should openly assume this responsibility. I feel sure that Dr. Blackader, whose name is associated with this lecture, would have approved of this because of the broad humanity and understanding which characterized his activities not only in pædiatrics but in all his work.

REFERENCES

1. ANDERSON, J. *et al.*: *Lancet*, 2: 720, 1954.
2. BOWLBY, J.: Child Care and the Growth of Love, Penguin Books Ltd., London, 1953.
3. BRAY, J.: *J. Path. & Bact.*, 57: 239, 1945.
4. DOUGLAS, J. W. B.: *Lancet*, 2: 440, 1951.
5. DYKES, R. M.: Illness in Infancy, Thesis, University of Glasgow, 1950.
6. GILES, C. AND SANGSTER, G.: *J. Hyg.*, 46: 1, 1948.
7. LIGHT, J. S. AND HODES, H. L.: *Am. J. Pub. Health*, 33: 1451, 1943.
8. MARRIOTT, W. M.: Infant Nutrition, Henry Kimpton, London, 1930.
9. MORGAN, H. DE R. AND LEDINGHAM, J. C. G.: *Proc. Roy. Soc. Med.*, 2: 133, 1908-09.
10. NEWSHOLME, A.: Supplement to the 39th Annual Report of the Local Government Board of Great Britain, 1909-10.
11. PETERMAN, M. G.: *J. Pediat.*, 41: 536, 1952.
12. POWERS, G. T.: *Am. J. Dis. Child.*, 30: 632, 1925.
13. SHANKS, R. A.: *Arch. Dis. Child.*, 24: 208, 1949.
14. SHANKS, R. A. AND STUDZINSKI, L. P.: *Brit. M. J.*, 2: 119, 1952.
15. STEVENSON, J. S.: *Brit. M. J.*, 2: 123, 1952.

RÉSUMÉ

Les derniers vingt-cinq ans ont vu se produire une révolution dans la pratique de la pédiâtrie dont l'aspect le plus important est, sans contredit, la diminution de la fréquence et de la mortalité des maladies infectieuses. Ceci s'applique, entre autres, à la fièvre scarlatine et, en général, aux infections à streptocoques; mais si le rheumatisme juvénile a décliné, les néphrites aiguës sont, par contre, aussi nombreuses qu'avant. Les sulfamidés et les antibiotiques ont largement contribué à cette amélioration qui, cependant, avait débuté bien avant 1935. Parmi les autres causes, il faut mentionner l'organisation de l'enseignement de la pédiâtrie, l'amélioration des services sociaux, des perfectionnements dans le nursing et l'hygiène et, enfin, un sens plus profond des responsabilités sociales. La découverte des vitamines a contribué à la disparition des maladies de carence, particulièrement le rachitisme. Il en fut de même pour le métabolisme du fer par rapport aux anémies hypochromiques. L'administration de solutés par voies sous-cutanée, intrapéritonéale ou intraveineuse, de même que l'usage courant des transfusions sanguines ont guéri nombre de maladies infantiles et sauvé plusieurs vies. Si les soins aux prématurés ont résolu bien des problèmes, ils en ont, par contre, posé de nouveaux, telle la fibroplasie rétrolenticulaire résultant de l'emploi prolongé d'oxygène en concentration supérieure à 40%. De même, l'emploi de plus en plus répandu du BCG a-t-il rendu l'épreuve à la tuberculine inutile. De nouvelles entités morbides sont apparues comme, par exemple, la méningite tuberculeuse chronique et l'hypertension dans le syndrome néphrotique, qu'on ne voyait jamais jadis, à cause de la terminaison uniformément fatale et rapide de ces maladies. D'autres, enfin, telles la maladie fibrokystique du pancréas et le groupe des désordres du métabolisme étaient totalement inconnues.

En Angleterre et au pays de Galles, la mortalité infantile a passé de 153 en 1900 à 28 en 1950. Ce progrès est le résultat de l'abaissement de la mortalité infantile de la fin du premier mois de vie à la fin de la première année. La mortalité de la période néo-natale s'est montrée beaucoup plus réfractaire et contribue maintenant pour 65% à la mortalité infantile totale.

Dans plusieurs pays, la mortalité post-natale est de moins de 10 par 1,000 naissances, de sorte que la morbidité constitue dans ces cas un index plus sensible, réalisant ainsi le souhait de Farr qui considérait l'enregistrement des maladies comme une contribution inestimable à la thérapeutique et à l'hygiène. En 1951, Douglas rapporta, après une enquête s'étendant à tous les niveaux de la société, qu'il existe une différence dans la mortalité et la morbidité de la première année de vie dans les différentes classes sociales. Il semble que les gens de la classe à l'aise aient bénéficié davantage des progrès de la médecine moderne que ceux des autres classes.

Le régime des nourissons ne semble plus présenter de problème, tant et si bien que l'allaitement maternel est devenu de plus en plus rare et que la nourrice de la période victorienne n'est plus concevable.

La ville de Glasgow eut pendant longtemps la triste réputation d'être un foyer de rachitisme. Le problème du logement (qui sévit encore d'ailleurs) en était la cause. En 1919, le Gouvernement commença la distribution gratuite de l'huile de foie de morue. Dès 1930, la maladie avait pratiquement disparu. Une enquête, faite en 1942 et basée sur les données radiologiques, sur la fréquence du cranio-tabes révéla que le plus grand nombre de cas se présentait chez les enfants de moins de six mois. Aucun cas ne fut trouvé passé l'âge de 10 mois. Depuis la distribution du lait évaporé national (National Dried Milk), employé pour l'allaitement artificiel et contenant environ 1,230 U.I. de vitamine D au litre, le craniotabes ne se rencontre plus que très rarement, chez quelques prématurés. Il n'est pas impossible même que certains enfants reçoivent une surcharge de vitamine D. L'hypercalcémie n'en est pas moins un phénomène assez rare et, lorsque la vitamine D est en cause, une simple abstinence pendant quelques mois suffit souvent à rétablir l'ordre des choses. Il est intéressant de noter que l'hypocalcémie a subi le même déclin que le rachitisme mais, cependant, la proportion de cas admis pour convulsions fut précisément la même pour la période de 1942-1946 qu'elle avait été pour celle de 1922-1926.

L'inutilité d'un séjour à l'hôpital devient évidente lorsqu'un petit malade, une fois guéri, est replongé dans le milieu qui a favorisé l'éclosion de sa maladie. L'analyse des circonstances conduisant à l'hospitalisation démontre qu'environ un tiers des malades médicaux sont admis pour des causes socio-économiques. La proportion des cas où le manque d'hygiène mentale est en cause devient effarante. La séparation de sa mère serait, pour l'enfant en bas âge, une des influences les plus néfastes dans ce domaine. M.R.D.

METASTATIC CANCER OF THE TESTIS

In a report from Columbus, Ohio, Wildermuth gives a gloomy but not hopeless picture of results of irradiation therapy in cases of metastatic testicular neoplasm (in 3 out of 33 cases, metastases were controlled), but draws attention to the use of Nitrofurazone in this condition. Nitrofurazone is a urinary antiseptic which on internal use produces testicular atrophy. It was given to a patient after a course of irradiation, in a dose of 1.5-2 g. daily. The resultant destructive effect on the seminiferous epithelium led to ablation of metastases and definitely prolonged life. It is suggested that Nitrofurazone, in spite of its tendency to produce vomiting and toxic neuritis, may be of value in the treatment of this condition.—*Radiology*, 65: 599, 1955.

THE ROLE OF THE SWIMMING POOL IN THE TRANSMISSION OF PHARYNGEAL-CONJUNCTIVAL FEVER

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AN EPIDEMIC of pharyngeal-conjunctival fever in Washington, D.C., in 1954 was recently reported by Bell[1] and co-workers at the National Institutes of Health, Bethesda, Maryland. The spread of this epidemic was largely associated with swimming pools, but direct transmission occurred readily in homes and in hospitals. From eye and throat washings, and stools from patients with the disease, the Type 3 APC (adenoidal-pharyngeal-conjunctival) virus was readily isolated in tissue cultures.

Previously, Cockburn[2] studied a similar epidemic in Greeley, Colorado, which occurred in August and September 1951, in which there was an "unusual combination of features consisting of acute conjunctivitis, vesicular pharyngitis, muscle pains, and pyrexia." In 13 out of 54 cases examined by the slit-lamp three weeks after onset, the corneæ were found to have small, whitish plaques one mm. or less in size. The preauricular lymph nodes were not significantly enlarged but the lymph nodes in the neck were involved. Most patients had temperatures of 102° F. to 105° F., and many had pains in the back, legs or neck. In some instances a diagnosis of poliomyelitis was made, but spinal puncture did not reveal any increase in the cells in the C.S.F. It was estimated that from 25 to 50% of children swimming in the pools developed the disease.

In the 1954 Washington epidemic of pharyngeal-conjunctival fever due to Type 3 APC virus, the symptoms described were similar to those of the Greeley epidemic, with the exception that no corneal opacities were seen in the affected eyes. The two epidemics were probably due to the same agent, however, since a study of eight paired sera from the Greeley epidemic showed a rise in antibody titre to the Type 3 virus.

In Toronto, in the first six months of 1955, about 20 patients with viral conjunctivitis were referred to one of us (H.L.O.) from the clinics of the teaching hospitals of the University of Toronto, and from oculists in private practice in the Toronto area. These patients were adults and their symptoms consisted of a unilateral follicular conjunctivitis during the first five days, followed by involvement of the second eye in most instances. Enlargement and tenderness of the preauricular node on the affected side were variable, but could always be elicited when the node was palpated. About half the patients developed corneal opacities in the affected eyes, and from washings from the conjunctival sacs of seven of these patients a cytopathogenic effect (CPE) was seen in tissue cultures of trypsinized monkey-kidney or in HeLa cells. Three of these strains were sent to the virus laboratories of the National Institutes of Health in Bethesda and were identified as belonging to the Type 3 APC group of viruses.[3]

Commencing the first week of August 1955, children who had been swimming in swimming pools were sent to us with a conjunctivitis similar to that which had been occurring in adults earlier in the year. The conjunctivitis was usually milder in children than in adults, but followed a similar course, occurring first in one eye, and then in the second after a period of three to five days. In only a few instances were corneal opacities seen in children, and these disappeared within a few weeks. Pharyngitis and fever were present in most children, with a temperature of 103-105° F. persisting for four or five days in many instances. Muscle pains were frequently complained of and catarrhal otitis media was a common complication.

The disease was obviously being transmitted in the swimming pools, and mothers on their own initiative kept their children away from the pools, with the result that the attendance at these centres was greatly reduced during the last two weeks of August.

VIRUS STUDIES

Rowe and co-workers[4] (1953) at the National Institutes of Health in Bethesda, Md., were the first to show the presence of latent virus in adenoid and tonsil tissue which had been removed during routine operations. This virus not only caused a cytopathogenic effect in these tissues grown in tissue culture, but also was capable of causing a similar effect in a variety of tissue culture cells. The most sensitive of

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these was the strain HeLa, an epithelial cell originally derived from a carcinoma of the cervix. At the present time there are at least eight immunologically distinct types of APC virus, five of which (Types 1, 2, 4, 5 and 6) have been recovered from adenoid and tonsil tissue. Type 8 is thought to be the cause of epidemic keratoconjunctivitis (Jawetz[5]) and Type 3 the cause of epidemic pharyngeal-conjunctival fever.[1] Types 2, 3, 4 and 6, when inoculated into the eyes of volunteers, have caused a follicular conjunctivitis.[6]

In the present epidemic, washings have been taken from the eyes and throats of more than 50 patients, and virus studies are continuing in the virus laboratory of the Hospital for Sick Children in conjunction with Dr. A. J. Rhodes. At this time the nature of the disease closely resembles that which occurred in Washington, D.C., in 1954 and was caused by infection with the Type 3 APC virus. The identification of three of our seven strains of virus isolated from adults in the spring of 1955 as Type 3, further suggests that the swimming-pool epidemic was due to this virus.

TRANSMISSION

Although the Toronto swimming pools were open throughout July, no cases of pharyngeal-conjunctival fever were brought to our attention from June 15 till the first week of August. For the next four weeks, children and adults with the disease were sent to us in increasing numbers from widely scattered areas of the city and province. In order to determine the importance of the swimming pool in the transmission of the disease, a house-to-house survey was made by public health workers in a single area surrounding one of the school swimming pools. The results of this survey are shown in Table I.

It will be seen from this table that 74 of the patients within the area surveyed were children who gave a history of having been in the swimming pool within six to ten days of the onset of their symptoms. Only six children with the disease in this area gave a history of swimming in another pool or in lakes remote from this area. Thirty-one developed the disease at home from children who had previously contracted it in the swimming pool. In a number of homes all members of the family, including the parents, contracted the disease.

TABLE I.

CASES OF PHARYNGEAL-CONJUNCTIVAL FEVER OCCURRING WITHIN A HALF-MILE RADIUS OF A NORTH TORONTO INDOOR SWIMMING POOL (AUGUST 1955).

Cases originating in pool (all children)	74
" " in pools elsewhere	6
" " from direct contact at home	31
No history of swimming or contact at home	1
Total cases	112

SYMPTOMS AND COMPLICATIONS

Pharyngitis, fever, malaise and muscle pains were complained of by most children. The conjunctivitis was sometimes absent or minimal in children, but was the main cause of discomfort in adults. Corneal opacities were seen with the slit-lamp in many adult eyes but were of rare occurrence in children. Adults seldom complained of a sore throat and none recalled any appreciable malaise or fever. Catarrhal otitis media was a common complication in children, 42 of the 104 in this area complaining of sore ears. The symptoms are summarized in Table II.

TABLE II.

SYMPTOMS OF PHARYNGEAL-CONJUNCTIVAL FEVER IN 112 PATIENTS (AUGUST 1955)

	Children (104)	*Adults (8)*
Sore eyes	68	7
Fever, malaise and muscle pains	75	2
Sore throat	63	1
Sore ears	42	

It will be seen from this table that all manifestations of the disease were not present in every patient. However, atypical cases were included in the survey only when they occurred in homes in which other members of the family were suffering from this disease. Thus the incidence of the disease was probably much higher than this survey indicates, since many atypical cases did not come to our attention.

DISCUSSION

The occurrence of an epidemic of pharyngeal-conjunctival fever is reported at this time in order to bring this disease to the attention of public health officers and medical practitioners in Canada. Virus studies will be reported upon at a future date, the washings having been taken from some patients in this series and from more

than 30 additional patients studied in the clinics of the Hospital for Sick Children and the Toronto General Hospital.

SUMMARY AND CONCLUSIONS

1. An epidemic of pharyngeal-conjunctival fever which occurred in the Toronto area in the spring and summer of 1955, and the spread of the disease in swimming pools and by direct contact, are described.

2. Symptoms of the disease varied, but typically consisted of unilateral or bilateral follicular conjunctivitis, preauricular adenopathy, pharyngitis, fever, malaise and muscle pains.

3. Catarrhal otitis media was the chief complication, occurring in 42 of 104 affected children in the area surveyed. Corneal opacities developed in many adults, but were rare in children.

4. The disease spread primarily in swimming pools and secondarily in the homes of affected children.

Mrs. Violet Simmons assisted in the survey of patients and in the compilation of statistics.

This study comprises part of the survey of ocular diseases of virus etiology under the National Health Grant 605-9-63.

REFERENCES

1. BELL, J. A. *et al.*: *J. A. M. A.*, **157**: 1083, 1955.
2. COCKBURN, T. A.: *Am. J. Ophth.*, **36**: 1534, 1953.
3. ORMSBY, H. L., FOWLE, A. M. C. AND COCKERAM, A.: *Canad. M. A. J.*, **73**: 710, 1955.
4. ROWE, W. P. *et al.*: *Proc. Soc. Exper. Biol. & Med.*, **84**: 570, 1953.
5. JAWETZ, E. *et al.*: *Am. J. Ophth.*, in press.
6. RYAN, R. W., O'ROURKE, J. F. AND ISER, G.: *Arch. Ophth.*, **54**: 211, 1955.

RÉSUMÉ

1. L'auteur décrit une épidémie de fièvre pharyngo-conjonctivale qui se produisit dans la région de Toronto pendant le printemps et l'été de 1955, et la propagation de la maladie par l'eau des piscines et par contact direct.

2. Bien que présentant une symptomatologie variable, la maladie typique comprenait une conjonctivite folliculaire unilatérale ou bilatérale, une adénopathie préauriculaire, de la pharyngite, de la fièvre, des malaises et de la myalgie.

3. La complication principale fut l'otite catarrhale moyenne, qui se produisit chez 42 des 104 enfants atteints, dans la région sous observation. Des opacités de la cornée se développèrent chez plusieurs adultes, mais rarement chez les enfants.

4. La maladie se propagea d'abord dans les piscines et, secondairement, dans les demeures des enfants malades.

M.R.D.

RAUWOLFIA ALKALOIDS IN MENTAL SYNDROMES*

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THE ROOT OF THE PLANT *Rauwolfia serpentina* Benth. has been used for centuries in India for the treatment of nervous and other ailments. In the market places it was called *"Pagla-Ka-Dacra"*, meaning "insanity herb".[1] But even in India the drug rested in medical oblivion until the late thirties when the beneficial effects in mentally ill patients were first reported in a scientific journal by Sen and Bose.[2] They noted in particular its influence upon "insanity and maniacal symptoms". About 10 years later, in 1943, Gupta *et al.*[3] described good results in a small number of varied psychopathological states. This observation, however, had no great impact on the west until studies of the hypotensive effects of the drug[4-6] drew attention to its concurrent tranquillizing influence, and brought to the fore the above-mentioned psychiatric observations. Hakim[7] in 1953 reported up to 51% recovery in psychotics treated with a preparation of rauwolfia and other herbs, and 80% recovery if electroshock was used as an adjunct. Recently studies have been published by Noce *et al.*[8] giving the impression of almost universal favourable results. In a more critical vein, Kline[9, 10] reports at least a high proportion of positive results. Tyhurst and Richman[11] have written of the favourable effects of the drug on ward management in 19 cases.

The present study is based upon observations made on mentally disturbed persons treated with rauwolfia derivatives within the last 15 months.

Method.—One hundred unselected patients, ranging in age from 20 to 70, received rauwolfia derivatives, particularly Serpasil (reserpine), in a combined oral and intramuscular form, ranging from 0.5 to 15 mg. per day, for a period ranging from one week to four months. Almost all patients were receiving psychotherapy concurrently, one to three hours weekly. Of the 100 patients, 65 had neurotic reactions, 20 manic-

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depressive psychoses, and 15 schizophrenic syndromes. Approximately half of the patients were hospitalized, the rest were outpatients.

All cases have been followed up for from three months to one year. It should be noted that all psychoses were either of recent origin or of recent remission. All patients were ambulatory. Blood pressure was taken twice daily in hospitalized patients, and once or twice weekly in outpatients. Liver function tests were done initially, but since no changes were observed or reported in the literature this was discontinued. Blood cells were studied systematically in 10 patients who had received rauwolfia alkaloids for more than 10 days. In five other patients the blood cells were examined before the administration of 2.5 mg. of the drugs intravenously, and one hour and four hours afterwards.

RESULTS

1. *General physiological effects.* – In almost all cases there was an average fall in blood pressure from 5 to 15 mm. Hg. This hypotensive effect was much less but more sustained and less variable than that noted with chlorpromazine.[12] In only two cases did marked weakness occur associated with low blood pressure, but the side-effects were minor and consisted only of some dizziness. The amount and rate of decrease depended more or less on the dosage and the kind of rauwolfia alkaloid used. With concentrated and fast-acting ones the fall manifested itself usually on the second to fourth day, and with slow-acting ones, on the 10th to 15th day.

A relative hypothermia was noted in a few cases. Appetite increased in most individuals treated with a moderate dosage of the drug. There were three cases of severe nausea and vomiting, in one of which the vomiting recurred each time the drug was resumed. Peripheral vasomotor disturbances, including flushing, occasional chills, and dryness of the mucous membrane, occurred in some cases treated with a dosage above 5 mg. daily, particularly in intramuscular form. In one case the first intravenous injection of 2.5 mg. of Serpasil provoked marked flushing and injection of the sclerae within half an hour, and this was followed by moderate non-pitting œdema of hands and face which subsided within 24 hours.

These observations confirm those of other authors who reported hypothermic, bradycardiac, and hypotensive activities of the drug associated with an increase in the secretory and motor activity of the intestinal tract.

The special study of the blood cells by the method noted above did not show any particular change attributable to rauwolfia alkaloids. The alkaloids did not appear to possess any barbiturate-potentiating effect clinically. It is to be noted that in cases treated with combined rauwolfia and chlorpromazine (see below) these two drugs apparently reinforced each other in some of their effects.

2. *Clinical results.*—In the 65 neurotic reactions, 20 manic-depressive psychoses and 15 schizophrenic syndromes treated with rauwolfia alkaloids, the results were as shown in Table I.

Results in neurotic reactions.—This included anxiety neuroses, anxiety hysteria, obsessive-compulsive neuroses, and one case each of premenstrual aggressive outbursts and adolescent maladjustment. *Anxiety states.* Sixty patients suffering from neurotic anxiety states received rauwolfia alkaloids, mostly Serpasil, in an average daily dose of 2 mg., for an average period of two months. Fifty of the above cases were treated either privately or as outpatients. None of the patients was receiving intensive psychotherapy. Thirty-seven cases showed no change; two cases showed marked, twelve moderate, and one slight improvement; eight cases became much worse. Among the latter cases five showed intensification of panic and anxiety attacks, and in three other cases a serious depressive state developed and required hospitalization. In two, electroshock therapy had to be instituted. The dosage did not appear to have much correlation with the aggravation of the underlying condition, since six of these patients were receiving only 1 mg. and two others 3 mg. daily.

The markedly and moderately improved patients experienced a considerable reduction in panic and anxiety and manifested what could be designated as a reorganization of the controlling powers of the organism and an increase in ego-strength. In some instances, particularly in two markedly improved patients, one of whom was suffering from acute episodes of homosexual panic states, the concomitant psychotherapy was quite meagre (once a week, supportive), and the striking improvement did not appear to be related to psychotherapeutic work as such.

The general impression was that one-fourth of the neurotic anxiety states responded very

TABLE I.

CLINICAL RESULTS OF ADMINISTRATION OF RAUWOLFIA ALKALOIDS

Diagnosis	*No. of cases*	*Improvement*				
		Marked	*Moderate*	*Slight*	*None*	*Aggravation*
(1) Neurotic reactions:						
Anxiety neuroses	60	2	12	1	37	8
Obsessive-compulsive	3			3		
Adolescent maladjustment	1		1			
Premenstrual aggression	1	1				
(2) Manic-depressive reactions:						
Mania	4	1	3			
Depression without agitation	12			2	8	2
Depression with agitation	4		2	1		1
(3) Schizophrenic reactions:						
Paranoid without agitation	8			1	7	
Paranoid with agitation	6	1	4	1		
Hebephrenia	1				1	
Total	100	5%	22%	9%	53%	11%

favourably to small doses of rauwolfia alkaloids. The criteria for the identification of those individuals who may respond favourably have not yet been defined.

Obsessive-compulsive and other neuroses.—In three cases of obsessive-compulsive neuroses slight improvement occurred, but it was difficult to attribute this betterment to the effect of the drug, particularly as one case relapsed while under treatment. One case of adolescent maladjustment with schizoid trends showed marked improvement in the form of increasing sociability, co-operativeness, and ability to form relationships. Finally, in one case of repeated and regular premenstrual aggressive outbursts, after only one month of treatment with 1 mg. of Serpasil daily, attacks ceased and have now been absent for four months.

Manic-depressive reactions.—Four patients showing maniacal and 16 showing depressive states received rauwolfia alkaloids in an average daily dose of 8 mg., in combined oral and intramuscular form, for an average period of one month. Of the four maniacal states, three showed moderate and one marked improvement. Three of the patients whose illnesses were more in the hypomaniacal range were discharged within a month and were maintained by the oral administration of the drug outside the hospital. However, in no case was the actual psychological structure of the maniacal state changed, although its intensity was much decreased.

Among the 16 depressed patients, four were markedly agitated and anxious; of these, two improved moderately and one slightly, while one became worse. None of the 12 non-agitated depressed patients improved; two cases were actually aggravated, one with bursts of delusional and hallucinatory activities, and the other with deepening of depression.

The general impression was that in agitated depression rauwolfia alkaloids are useful in alleviating somewhat the agitation and excitation, permitting better ward management. In depression without agitation the drug appeared contraindicated, because it appeared to provoke added apathy and immobility in already inhibited individuals. In addition, it should be noted that three neurotic patients, as mentioned above, became markedly depressed.

Schizophrenic reactions.—Fourteen paranoid schizophrenics and one patient with a hebephrenic syndrome were treated with an average daily dose of 10 mg. of combined oral and intramuscular form of rauwolfia alkaloids, particularly reserpine, for an average period of 1½ months. Four cases were under treatment for four months. There was marked improvement in one agitated paranoid and moderate improvement in four other excited and anxious patients. However, the improvement in the latter four was not sustained and they had to receive other forms of treatment. No significant changes were noticed in the other schizophrenic cases.

The general impression was that, as with neurotics, some particular schizophrenic reactions may respond very favourably to rauwolfia alkaloids, but the mode of selection of such cases is at present unknown and is worthy of further investigation.

COMBINED CHLORPROMAZINE AND RESERPINE TREATMENT

Four patients with anxiety neuroses, one in a mixed state of depression and excitation, one hypomanic, and one borderline psychoneurotic with schizoid features received chlorpromazine and reserpine in an average daily dose of 100 mg. and 3 mg. respectively for an average period of three weeks. The four anxiety neurotics all showed some improvement within two weeks. The hypomanic improved markedly and was discharged in two weeks. The borderline psychoneurotic and the patient in a depressive state became worse; the former manifested increasing withdrawal and depression, and the latter became acutely psychotic with delusional and hallucinatory phenomena within one week. Because we have not observed aggravation of symptoms with chlorpromazine,[12] it can be inferred that the rapid worsening of the case was perhaps due to the activating effect of the two drugs.

It appears from this short series, and from our previous experience with chlorpromazine, that the combination of the two drugs necessitates the lowering of the dosage to modify the side-effects, which consisted mostly of dizziness, weakness, somnolence, and drop in blood pressure. This drop in blood pressure was quite marked in two cases within 12 hours: in one case it fell from 140/85 to 96/50 mm. Hg, and in the other from 180/90 to 90/70. The rapid recovery of the hypomaniacal patient and improvement of the anxiety states indicate very probably that the two drugs may have a summation and facilitatory effect which may be useful in shortening the duration of excitatory and maniacal states.

COMPLICATIONS

Excluding the side-effects noted as a part of the general physiological effects of the drug in some cases, there were few serious complications. Incapacitating nausea and vomiting occurred in one case, transient ankle œdema in two cases during the first and the second week of treatment, slight tremor of the upper extremities in one case, and a mild extrapyramidal syndrome, resembling Parkinson's syndrome, in one case. The paucity of extrapyramidal complications is worthy of note, in contrast to the relatively high incidence of 12 instances in a series of 19 cases reported by Tyhurst and Richman[13] from this institute.

COMMENTS

The over-all analysis reveals that 27% of all cases showed improvement, 5% marked and 22% moderate; 62% showed no appreciable change (in this the 9% slightly improved cases are included); in 11% symptoms were aggravated. It should be noted that in no instance, even in the markedly improved cases, was the actual psychological structure of the mental syndrome altered. What happened in improved cases might be called an ego- or self-distancing from the disturbing and emerging symptoms, affects, and painful and energy-consuming restitutional activities. We do not consider this, as others have done, to be proof of a reorganizational effect of rauwolfia alkaloids. We assume it to be a non-specific effect of the drug in breaking the event-chain[14] of the disease at some particular point in the organismal sequence; here probably at the position of excitation and anxiety. This effect is similar clinically to the one produced by chlorpromazine. However, chlorpromazine appears to have a more powerful, less diffuse, and more specific action. With chlorpromazine, 20 out of 27 anxiety neurotics showed moderate to marked improvement,[12] while with rauwolfia alkaloids the incidence in similar cases was 14 out of 60.

Our general positive clinical results with rauwolfia derivatives were meagre in comparison with the ones obtained by Noce *et al.*, who declared that all cases improved. Kline reported improvement in 61.1% of cases. Because of the importance which this drug has acquired in the medical and public mind for the treatment of mental disorders, some attempt to explain the discrepancy in reports is in order. The difference between our results and those of others may be viewed from several angles, the most important of which appear to us to be the patient population, the therapeutic setting and the level of the expected psychological recovery. Our investigation was carried out either in an open psychiatric institute, in an out-patient clinic, or in private practice, where excitation and behavioural disturbances were relatively mild or of recent origin, and where the expectation of psychological recovery was relatively high. In these particular settings small changes which would

have made a great difference in a closed, chronic hospital are not viewed as significant, are not taken as indicating recovery or improvement, and do not provoke enthusiasm comparable with that experienced by those who for years have been struggling with "agitated wards" and welcome any alleviation of tension. That is to say, the positive value of quietening a rowdy patient in a chronic hospital may mask the true therapeutic evaluation in terms of psychodynamic change.

The discrepancy of results cannot be explained by the dosage or the length of the therapy, because our dosage and length of treatment were comparable with those of other investigators. At this point something should be said about the 11 cases showing aggravation. The concept of a "turbulent phase" leading to a "reorganization" phase[10] may explain this phenomenon, but since the so-called turbulent phase did not occur in the other 89 cases, some of which were treated for more than four months, we are inclined to minimize the explanatory value of this suggestion. In addition, in three cases deep depression, inhibition, apathy, and immobility resulted rather than turbulence. The turbulent phase, if it occurs, may be considered, at least in some cases, to be an acute toxic psychotic state comparable to many other drug-provoked acute psychoses. Besides, it would be difficult to find a psychodynamically valid argument to substantiate the contention made by Kline *et al.* that a sudden and unprepared breaking through of defences (or what appears to be so), outside an appropriate psychotherapeutic setting, with subsequent flooding of the psychological field by unconscious need systems and drives, will have a reorganizing effect on personality structure. It may be argued that this may have, on the contrary, a detrimental effect on the existing ego structure, such as occurs in some people after drug-induced psychoses for experimental purposes, who show lasting unfavourable results.

For the above reasons, and from the clinical results of this study, it can be concluded that the range of therapeutic efficacy of rauwolfia derivatives in mental syndromes is limited, and that much care must be exercised in first assessing the alterations of psychodynamic structure of the syndrome under study before putting forward hypotheses and before letting our enthusiasm run the vehicle of scientific accuracy. However, because of some, almost unexpected, good results in a few cases, it appears necessary to determine criteria for the selection of cases suitable for rauwolfia therapy.

SUMMARY

1. One hundred unselected patients received rauwolfia alkaloids in combined oral and intramuscular form, in a daily dose ranging from 2 to 10 mg., for a period of time ranging from three weeks to four months. These patients included 65 neurotics, 20 manic-depressives, and 15 with schizophrenic reactions. All cases were followed up for from three to 12 months.

2. Of the neuroses, three showed marked, 13 moderate, and four slight improvement; 37 cases showed no change, and eight became worse. Aggravation manifested itself as deep depressive states in three patients who required hospitalization and electroshock treatment, and increase in anxiety and panic attacks in five other cases.

Of four patients with maniacal states, one showed marked and three moderate improvement. Only two out of 16 patients with depression showed improvement, and three became worse.

Of 15 schizophrenics, one showed marked and four moderate improvement. The latter patients, however, had to receive electroshock therapy later. The general impression was that the non-agitated depressive states and hebephrenic reactions were relative contraindications to rauwolfia therapy.

3. Four patients with anxiety neuroses, and one each with depression, hypomania, and borderline psychoneurosis received a combination of chlorpromazine and reserpine. Both drugs appeared to activate each other's tranquillizing effect, but it seemed that chlorpromazine enhanced the toxic manifestations of reserpine.

4. Complications were met with in a few cases; there was one case of intractable vomiting, two of transient ankle œdema, one of slight tremor of the upper extremities, and one of a Parkinson-like syndrome.

5. The over-all analysis revealed that 27% of all cases showed from marked (5%) to moderate (22%) improvement; 62% manifested no change, and 11% became aggravated. The favourable clinical results appeared meagre in comparison with the ones reported by others. The possible reasons for this discrepancy are discussed. It is maintained that the difference in

patient population, therapeutic setting, and the level of expected psychological recovery between an open and a chronic hospital may be responsible for this divergence. Much caution is recommended against undue enthusiasm and premature theorizing. It is concluded that the therapeutic efficiency of rauwolfia derivatives in mental syndromes is very limited. However, because of some almost unexpected good results in a few cases, it appears necessary to determine a way for the selection of such cases, if such there be.

The authors acknowledge their deep appreciation to the members of the staff of the Allan Memorial Institute of Psychiatry for their kind co-operation and forwarding of necessary data.

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REFERENCES

1. CHOPRA, R. N., GUPTA, J. C. AND MUKHERJEE, B.: *Indian J. M. Res.*, 21: 261, 1933.
2. SEN, G. AND BOSE, K. C.: *Indian M. World*, 2: 194, 1931.
3. GUPTA, J. C., DEB, A. K. AND KAHALI, B. S.: *Indian M. Gaz.*, 78: 547, 1943.
4. VAKIL, R. J.: *Brit. Heart J.*, 11: 350, 1949.
5. WILKINS, R. W.: *Ann. Int. Med.*, 37: 1144, 1952.
6. *Idem*: *Ann. New York Acad. Sc.*, 59: 36, 1954.
7. HAKIM, R. A.: Indigenous drugs in the treatment of mental disease. Read before the Sixth Gujrat and Saurashtra Provincial Medical Conference, Baroda, India, 1953.
8. NOCE, R. H., WILLIAMS, D. B. AND RAPAPORT, W.: *J. A. M. A.*, 156: 821, 1954.
9. KLINE, N. S.: *Ann. New York Acad. Sc.*, 59: 107, 1954.
10. *Idem*: Clinical applications of reserpine. Presented at Am. Psychiat. A. meeting, Section in Medical Science, Berkeley, 1954.
11. TYHURST, J. S. AND RICHMAN, A.: *Canad. M. A. J.*, 72: 458, 1955.
12. AZIMA, H. AND OGLE, W.: *Ibid.*, 71: 116, 1954.
13. RICHMAN, A. AND TYHURST, J. S.: *Ibid.*, 72: 457, 1955.
14. CAMERON, D. E.: *Science*, 107: 553, 1948.

RÉSUMÉ

1. A cent malades pris au hasard, on administra des alcaloïdes de Rauwolfia, par voie combinée orale et intra-musculaire, en doses quotidiennes variant de 2 à 10 mgm., pendant une période s'étendant de 3 semaines à 4 mois. Parmi ces patients se trouvaient 60 névrosés, 20 cyclothymiques, et 15 schizophrénes. Tous les cas furent surveillés pendant une période de 3 à 12 mois.

2. Parmi les névrosés, 3 furent considérablement améliorés, 13 présentèrent un progrès satisfaisant, et 4 une légère amélioration; 37 n'accusèrent aucun changement, et l'état de 8 d'entre eux s'aggrava. Cette aggravation se manifesta par de graves dépressions chez 3 patients qui durent être hospitalisés et recevoir des électrochocs; par une angoisse accrue et des attaques de panique chez les 5 autres. Sur 4 maniaques, 1 fut remarquablement amélioré et 3 présentèrent un progrès satisfaisant. Des 16 mélancoliques ayant été traités, 2 seulement furent améliorés tandis que l'état de 3 d'entre eux s'aggrava. Quinze schizophrènes reçurent du Rauwolfia; 1 fut grandement amélioré et 4 présentèrent un progrès satisfaisant. Toutefois, ces derniers durent plus tard recevoir des électrochocs. L'impression générale fut que les états dépressifs non-agités et l'hébéphrénie constituent des contre-indications à la thérapie par le Rauwolfia.

3. A 4 patients atteints d'anxiété, à un mélancolique, à un hypomaniaque et à un patient atteint de désordre frisant la psychonévrose, on administra une combinaison de chlorpromazine et de réserpine. Chacune des deux drogues sembla augmenter l'effet calmant de l'autre, bien que la chloropromazine parut accentuer les manifestations toxiques de la réserpine.

4. Quelques patients présentèrent des complications: un cas de vomissements incoercibles, deux cas d'œdème transitoire des chevilles, un cas de tremblement léger des extrémités supérieures, et un syndrome rappelant celui de Parkinson.

5. L'analyse de tous les cas révèle que 27% présentèrent une amélioration: remarquable dans 5% d'entre eux, et modérée dans 22%; 62% n'accusèrent aucun changement. L'état de 11% s'aggrava. Les bons résultats cliniques semblent minces en comparaison de ceux rapportés ailleurs. Les raisons possibles de cette contradiction sont mises en évidence: la différence dans le genre de malades, le milieu thérapeutique, et la différence entre le taux de guérison psychologique, dans un institut de psychiâtrie ayant un dispensaire et dans un hôpital pour maladies mentales chroniques.

On met en garde contre l'enthousiasme exagéré et les théories prématurées. En conclusion, il appert que la valeur thérapeutique des dérivés du Rauwolfia dans les syndromes mentaux est très limitée. Cependant, à cause de quelques bons résultats presque inattendus, il semble nécessaire d'établir une méthode pour reconnaître les cas qui pourraient bénéficier d'une telle thérapeutique.

M.R.D.

THE USE OF KIELLAND'S FORCEPS

This discussion was introduced by Dr. Parry-Jones, who pointed out that when Kielland's forceps were developed it was expected that they would be used for high forceps cases, whereas now the question arose whether they offered advantages for delivering a head already engaged in the pelvis. He was convinced that Kielland's forceps had great advantages. They provided a gentle and simple method of rotation and permitted axis traction. When manual rotation was difficult or impossible, Kielland's forceps were indicated but they must be used by an experienced operator. Much practice was needed and Kielland's forceps should not be kept in a cupboard until a really difficult case was encountered.

Dr. Parry-Jones discussed the three methods of applying the forceps: (1) the classical method; (2) the wandering method; (3) the direct method. There were indications for all three, but the wandering method could be used in almost every case. With the blades in position an attempt should be made to rotate the head before undertaking traction, which should always be in the line of the handles, with only two fingers used. Rotation and traction should never be carried out together. The special risks associated with Kielland's forceps were: (a) injury to the bladder; (b) third-degree tear; (c) rupture of the lower segment. Combined figures were given for two maternity hospitals and for a personal series. No maternal death was recorded and there was a gross fetal mortality of 5.7% corrected to 1.9%.

The next speaker, Dr. Gunn, had used Kielland's forceps for 24 years, not only for posterior positions, but also by direct application in anterior positions. He stressed the need for constant practice with them. He analyzed the 21 fetal losses in 186 rotation cases, the worst of a series of 14,000 deliveries. He advised any obstetrician who was prepared only to use the forceps in occasional cases to take them home and use them for putting coal on the fire.—E. Parry-Jones and A. Gunn, *Proc. Roy. Soc. Med.*, 48: 681, 1955.

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THE COBALT BOMB IN THE TREATMENT OF BLADDER TUMOURS

A PRELIMINARY REPORT

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THE COBALT-60 Beam Unit was first put into operation at London, Ontario, in November 1951 under the direction of Dr. Ivan Smith of the London Clinic of the Ontario Cancer Foundation. This became the first unit of its type in the world to treat patients, and as of May 1955 58 primary bladder tumour cases have been treated with this unit. The term "cobalt-60" stands for the atomic weight of this particular isotope of cobalt used as the source of gamma ray radiation. In this case the cobalt is in the shape of two discs approximately the size of two 50-cent pieces. It is interesting to note that they have just been replaced in May 1955 from the Chalk River plant. The strength of this unit is approximately the same as a 2,000,000-volt x-ray therapy machine. The tremendous advantage of the cobalt bomb type of radiation is that only two gamma rays are emanated and these of almost identical wave lengths, a monochromatic beam, so that there is none of the scatter which occurs in a powerful x-ray unit with a broad spectrum of emanation. Skin reactions were so slight as to be entirely overlooked, since the maximum effect of the rays is not on the skin surface but situated about 6 mm. below it. In the beginning no one was too sure of the types of reactions, or the value of the result to be obtained, so that progress was slow and cautious. However, there was a totally unprecedented amount of publicity connected with the early work of the cobalt bomb as a result of one magazine article, and people came and requests for treatment poured into the Clinic from all over North America.

One most important point should be brought out and emphasized at this time. Dr. Ivan Smith and his staff have felt that, even though this treatment might be considered a straw to offer the desperate, they could not be responsible for refusing it and they would treat, on a palliative basis if necessary, anyone who came from a referring physician and on whom suitable information could be obtained for accurate evaluation of the extent of tumour and dosage to be given if possible. Even so, many had to be discouraged from coming for treatment as it was felt the tumour had spread too far—a difficult decision to make at times and involving innumerable telephone conversations, correspondence and hours of thought. This policy has been criticized, rightly or wrongly, by many, and therefore it is with considerable interest that the present series of 58 cases have been reviewed and are being presented here. The cobalt bomb was used 18 hours a day with the staff on a staggered-shift system, in order to hold up no one's treatment and handle as many cases as it was felt possible to treat. It was not an unusual sight to see these patients being wheeled off to the Cancer Clinic at any hour, early or late, from 6 a.m. to 10 p.m.

The majority of these cases were poor cases for irradiation therapy, or any other type of treatment for that matter, by the very extent of the lesion. These people were mostly found to have big lesions, and consequently were being faced with possible resection of large segments of bladder, ureteral transplants with cystectomy, and even more radical surgical procedures or this new form of irradiation therapy, as a possible alternative. If the surgeon felt that there was a reasonably good chance of curing them by operation, irradiation was not considered too strongly. It therefore becomes evident that some very difficult therapeutic problems arose.

Many of these patients arrived for investigation and treatment in poor condition, dehydrated, septic with grossly infected urine, and exhausted from loss of sleep. These patients were hospitalized when possible for supportive therapy, blood studies, pyelography and search for metastases, and antibiotics after urine cultures. Patients in better condition were usually treated as outpatients. The pathological sections were reviewed and reported on by Dr. J. H. Fisher, Professor of Pathology at the University of Western Ontario and Chief of the Pathology Department at Victoria Hospital, London. Cystoscopy was carried out when possible with a member of the Cancer Clinic present to review the location and size of the lesion and check the results of bimanual examination. In many cases stereocystograms were made with 100-150 c.c. of contrast medium injected into the bladder; skin markings and lead markers were located so that upon viewing the films the lesion could be

reasonably well located. Because of the lack of skin reactions, once the markings were done and the patient cautioned not to bathe or wash them off, localization for the cobalt bomb was not a problem. Cystograms were not always made if the patient was of the thin body type, particularly during the later years of cobalt bomb therapy.

The patient was then presented by the member of the Cancer Clinic assigned to him and discussed at one of the daily Cancer Clinic conferences. The entire problem was reviewed, a decision being made as to the need for hospitalization, antibiotics, regular white cell counts, and the total dosage and the number of ports to be treated.

COBALT-60 BEAM THERAPY — GENERAL DATA

Fifty-eight patients were treated, aged 39 to 88 (average 61.6 years). There were 45 men and 13 women. Symptoms before therapy had lasted for 1 to 60 months. Tumour types: transitional cell 33; papillary 11; squamous cell 8; anaplastic 6.

Actually more than this number of patients received cobalt therapy, but in some it had stopped within a few days or had just finished prior to this report, and it was felt that the dosage received was too small or the treatment completed so recent that there was no value in including them.

Palliative therapy.—3,000 r-4,000 r in 3-4 weeks. Thirty-four cases were treated. Twelve had reactions and 14 relief of symptoms (bleeding, frequency, dysuria). Seven are alive and three free of tumour.

An effort has been made to be very fair and include in the number of reactors anyone complaining about his bladder. Usually in these cases only two ports of irradiation were used, anterior and posterior parallel ports.

Radical therapy.—5,000 r-6,000 r in 3-6 weeks. There were 24 cases and 16 reactions. Sixteen were relieved of their symptoms; 13 are alive and five free of tumour.

The trend during the later months of this report was to try to give a higher dosage through four ports and in a longer period of time up to 6½ weeks. The economic factor of the patient's being required to remain for such a prolonged period sometimes became a real problem, and required discussion before the programme of dosage was initiated.

SELECTED CASES

I have chosen to discuss in some detail only 12 of these 58 cases, and have divided them into three groups. *First:* Those who did badly or died, we believe, as a result of their therapy. *Second:* Those about whom we felt that there was definitely something to offer, and who did well. *Third:* Those who proved a pleasant surprise to us after therapy.

First Group

Mrs. H.G. (72 years). *First symptom* (December 1952) frequency and dysuria, never a gross hæmaturia. *Cystoscopy* (January 1953). Large posterior wall tumor, very hard. Had to use resectoscope to biopsy. *Pathological report.* Epidermoid carcinoma into muscle. *Cystotomy* (January 1953). Tumour through peritoneum into small bowel adherent to it. *Interval from first symptom to cobalt therapy* 1 month. January 1953: Cobalt 4000 r in 4 weeks. February 1953: fistula to skin; severe leg pains. March 1953: Died. Post mortem, no viable tumour.

From this case we learned an extremely valuable lesson that these cases must not be irradiated too soon after cystotomy has been performed. The pathological studies revealed no viable tumour in the bladder, but a large hole had sloughed out of her bladder through the peritoneum and included the extension area of tumour into loops of small bowel adherent to the posterior bladder wall.

Mrs. E.E. (74 years). *First symptom* (January 1952) frequency and dysuria. Cystoscopy and biopsy (July 1952); right lateral wall tumorous mass. *Pathological report*: Papilloma with malignant change. *Interval from first symptom to cobalt therapy* 11 months. December 1952: sent for cobalt therapy, 5000 r in 4 weeks; diarrhœa and frequency during treatment. March 1953: cystoscopy; shrivelled-up stump; symptomatically a lot better. May 1953: cystoscopy and biopsy; ulcerated area. *Pathological report*: Infiltrating Grade III tumour. Symptoms worsened—cystoscopy revealed a large ulceration. June 1953: cobalt 4000 r in 4 weeks. September 1953: condition worse with frequency and dysuria. October 1953: ureteral transplantation refused. October 1953: died.

Although this patient was clinically definitely better and her bladder improved as seen on cystoscopic examination after her first course of cobalt therapy, her condition worsened after the second course.

Mr. H.S. (56 years). *First symptom* (June 1952) dysuria and frequency. September 1952: one tiny clot noted in urine. November 1952: cystoscopy; large right-sided tumour; intravenous pyelography; non-visualization on right. December 1952: cystoscopy and biopsy. *Pathological report*: transitional Grade IV tumour. *Interval from first symptom to cobalt therapy* 6 months. January 1953: cobalt 5000 r in 3 weeks; frequency, etc. but didn't complain; carried as outpatient. February 1953: died suddenly of uræmia. Post mortem, not much bladder left; no viable tumour.

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This patient was treated as an outpatient and he was in a much more extreme state than was realized. He actually developed a necrotizing cystitis, and the whole lining of his bladder sloughed out. Subsequently all outpatients were questioned closely and the urine specimens checked regularly.

Mr. P.B. (60 years). *First symptom* (July 1953) frequency and dysuria. September 1953: hæmaturia. September 1953: cystoscopy; large right-sided tumour. October 1953: suprapubic exploration—large right-sided mass outside bladder. *Pathological report:* Papillary Grade III tumour. January 1954: palpable mass outside bladder; referred for cobalt therapy. January 1954: cystoscopy; gross large right-sided tumour. *Interval from first symptom to cobalt therapy* 6 months. February 1954: cobalt 5500 r in 4 weeks; reaction; put in hospital. June 1954: cystoscopy; still tumour present, symptomatically good. August 1954: cystoscopy; still tumour present. October 1954: cobalt 2000 r to iliac fossa; hospitalized with pain and œdema. November 1954: downhill; vesical fistula and bowel fistula. December 1954, died.

Initially this man's condition improved but his subsequent course was tragic, with a fistula developing from bladder to skin and later bowel also. This would appear to have been just too large a mass to handle by irradiation therapy. It had been felt that there was nothing else to offer him, however.

Second Group

Mr. J.D. (65 years). *First symptom* (spring 1951) frequency. July 1951: segmental resection and suprapubic fulguration. *Pathological report*: adenocarcinoma. Four recurrences—each time cystoscopy and fulguration. *Interval from first symptom to cobalt therapy* 8 months. October 1952: cobalt 5000 r in 3 weeks. October 1952: cystoscopy and tumours fulgurated; little reaction till one week. January 1953: cystoscopy; first time clear since July 1951. July 1953: cystoscopy and biopsy negative. All clear since then.

This man had multiple bladder tumours which were not being adequately controlled by electrocoagulation. These cases were believed to be well handled by irradiation therapy and his subsequent course would appear to bear this out.

Mrs. M.A. (59 years). *First symptom* (September 1952) frequency. October 1952: hæmaturia. January 1953: cystoscopy; large left-sided tumour; referred for cobalt therapy. January 1953: cystoscopy; movable tumour; resected transurethrally, with broad base including left ureteral orifice; base of bladder resected. *Pathological report*: Anaplastic Grade IV tumour. *Interval from first symptom to cobalt therapy* 5 months. February 1953: cobalt 5500 r in 3 weeks; some diarrhœa, a little frequency. Regular 3-monthly cystoscopies since then. Intravenous pyelography negative. All clear.

This patient had a high-grade tumour extending into bladder musculature and involving her ureteral orifice. Her post-irradiation result has been most gratifying.

Mr. F.C. (61 years). *First symptom* (August 1953) hæmaturia; cystoscopy—cystitis. September 1953, frequency and dysuria. November 1953, intravenous pyelography: some bilateral hydronephrosis. *Cystoscopy* posterior wall tumour. *Pathological report*: Anaplastic carcinoma. *Interval between first symptom and cobalt therapy* 4 months. December 1953, cobalt 4450 r in 40 days—2 short courses due to reaction. January 1954, terrible bladder reaction—strangury to point of incontinence; jaundiced, palpable liver, NPN rose. February 1954, cystoscopy: 2 areas of slough; capacity now 6-7 ounces. September 1954, cystoscopy negative. April 1955, cystoscopy negative.

This man's tumour was on the posterior wall, and hydroureters were seen on an I.V. pyelogram. It was suspected that the tumour extended well into the bladder wall and that the surgical prognosis was poor. Although he nearly died from cobalt therapy, he has survived and is clinically tumour-free.

Mr. P.M. (74 years). *First symptom* (December 1952) hæmaturia. June 1953, suprapubic prostatectomy and diverticulectomy with tumour in diverticulum. *Pathological report*: Papillary Grade II tumour. May 1953, cystoscopy—anterior neck tumour. *Interval from first symptom to cobalt therapy* 5 months. May 1953, cobalt 6000 r in 33 days—some bleeding and frequency. August 1953, cystoscopy—tumour all shrivelled up; asymptomatic. Regular cystoscopies all clear.

This man almost died at the time of his anæsthesia and last transurethral attack upon the tumour. It was felt that no further anæsthesia or surgical procedure could be carried out and therefore only some type of irradiation was possible. He has done extremely well clinically.

Third Group

Mr. H.G. (65 years). *First symptom* (Sepember 1952) hæmaturia and dysuria. September 1952, transurethral resection. *Pathological report*: Transitional Grade III tumour, left base; intravenous pyelography negative. March 1953, cystoscopy—recurrence fulgurated. July 1953, cystoscopy—recurrence fulgurated, left vesicopelvic thickening. January 1954, cystoscopy — recurrence fulgurated. Intravenous pyelogram: right kidney not visualized, left hydro-ureter. *Time between first symptom and cobalt therapy* 17 months. January 1954, cobalt 3450 r in 3½ weeks—some incontinence of urine. August 1954, symptom-free. Cystoscopy negative. February 1955, cystoscopy negative.

A long, bad history with what was felt to be definite extension outside the bladder to the pelvic wall, therefore a poor surgical prognosis. A rather amazing result when his small dosage of cobalt is noted.

Mr. H.M. (71 years). *First symptom* (December 1953) hæmaturia intermittently for 3 years. January 1954, cystoscopy—multiple papillary tumours and sessile

tumours. January 1954, suprapubic cystotomy—resection and fulguration. *Pathological report*: transitional cell tumour into muscle. February 1954, cystoscopy—multiple tumours. *Interval from first symptom to cobalt therapy* 38 months. February 1954, cobalt 5750 r in 4 weeks—little reaction. May 1954, cystoscopy—multiple tumours, some regression in size. June 1954, multiple tumours—some regression in size; jaundiced, ? big liver with metastases. October 1954, cystoscopy: unchanged—nodule in scar of suprapubic approach. January 1955, scar nodule enlarged. March 1955, cystoscopy and fulguration—later excision of nodule (bladder tumour).

This man went for over a year following cobalt therapy with no attempt made to treat the numerous tumours present in his bladder. They were observed to shrivel up but not to disappear. Subsequent electrocoagulation and transurethral resection appear to have controlled them adequately, but the time is too short to be sure.

Mr. H.T. (54 years). *First symptom* (July 1953) dysuria. August 1953, hæmaturia. October 1953, cystoscopy—left posterior wall fulgurated. March 1954, suprapubic cystotomy and fulguration. *Pathological report*: transitional cell carcinoma. March 1954, cystoscopy—raw sloughing areas on anterior wall and posterior wall. *Interval from first symptom to cobalt therapy* 9 months. April 1954, cobalt 6450 r in 6½ weeks—little reaction. July 1954, cystoscopy negative. October 1954, cystoscopy negative; weight regained; asymptomatic. December 1954, cystoscopy negative. March 1955, cystoscopy negative.

This man was treated by the method now believed to be best—namely by a high dosage 6000 r plus, and over a longer period of six to seven weeks. He tolerated the large dosage well and is doing very nicely.

Mrs. M.S. (71 years). *First symptom* (March 1953) frequency and dysuria. February 1953, cystoscopy—multiple sessile tumours—biopsy and fulguration. *Pathological report*: transitional Grade II tumour. March 1954, cystoscopy—one tumour left in dome, remainder fulgurated. *Interval from first symptom to cobalt therapy* 12 months. March 1954, cobalt 6325 r in 6½ weeks. August 1954, cystoscopy negative; excellent result symptomatically. February 1955, cystoscopy negative.

This patient with multiple bladder tumours was treated with large dosage, 6000 r plus, in over six weeks' time. There was no reaction and the post-therapy result was excellent.

CONCLUSIONS

I feel that the number of patients (58) and the time interval (less than 5 years) do not allow any definite conclusions to be drawn. The following important facts should be kept in mind at all times in future similar therapy.

1. Irradiation should not be carried out earlier than three weeks after bladder opening to expose or biopsy the tumour.

2. Daily or at least twice weekly, urine should be examined clinically, and reported upon during the treatment period.

3. Large necrotic tumour masses with the usual complication of a grossly infected urine tend to have a poor course during therapy. An attempt should be made to reduce the amount of necrotic tissue on the surface of the tumour and clear up the urine with antibiotics by means of routine culture and sensitivity studies.

4. Cobalt therapy has a definite place in the treatment of bladder tumours. It should be kept in mind for patients who refuse operation or on whom it is felt unsafe to carry out a long complicated surgical procedure.

5. Multiple bladder tumours which have responded poorly to electrocoagulation have been controlled well by the cobalt bomb.

It is sincerely hoped that when a five-year period has elapsed in a sufficient number of cases of cobalt bomb therapy for bladder tumours, a more detailed and valuable report may be published.

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RÉSUMÉ

L'auteur décrit la bombe au cobalt de la London Clinic of the Ontario Cancer Foundation, à London, Ontario. Les traitements, sous la direction du Dr. Ivan Smith, sont administrés, soit comme palliatif, soit comme une dernière tentative dans les cas désespérés. Depuis novembre 1951, cinquante-huit cas de cancer de la vessie reçurent des radiations. L'auteur présente 12 de ces 58 cas; il les divise en trois groupes, au point de vue des résultats: 4 mauvais, 4 assez bons, et 4 bons.

Le nombre des patients (58) n'est pas assez grand et l'intervalle (moins de 5 ans) trop court pour justifier des conclusions certaines. Pour l'avenir de la thérapie par la bombe au cobalt, il faudrait toujours se rappeler les importants faits suivants.

1. L'irradiation ne devrait jamais être administrée moins de trois semaines après l'ouverture de la vessie pour reconnaître la tumeur ou pratiquer une biopsie.

2. Chaque jour, ou au moins deux fois par semaine, on doit pratiquer une analyse d'urine et en faire rapport pendant la durée du traitement.

3. Les grosses tumeurs nécrosées, sources de pyurie, se comportent mal pendant le traitement. Il faut chercher à débrider le plus possible le tissu nécrotique superficiel et nettoyer l'urine avec un choix d'antibiotiques basé sur des cultures bactériologiques répétées et des observations de la sensibilité des microbes incriminés.

4. La thérapie au cobalt a une place bien établie dans le traitement des tumeurs de la vessie. On doit y songer pour les malades qui se refusent à l'opération ou qui ne sont pas en état de la subir

5. Certaines tumeurs multiples de la vessie, qui avaient résisté à l'électrocoagulation, ont été jugulées par la bombe au cobalt.

L'auteur espère reprendre ce travail in extenso lorsqu'une période de cinq ans se sera écoulée chez un plus grand nombre de cas ayant reçu des radiations de la bombe au cobalt.

M.R.D.

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THE PRESENT STATUS OF ALDOSTERONE IN CLINICAL MEDICINE*

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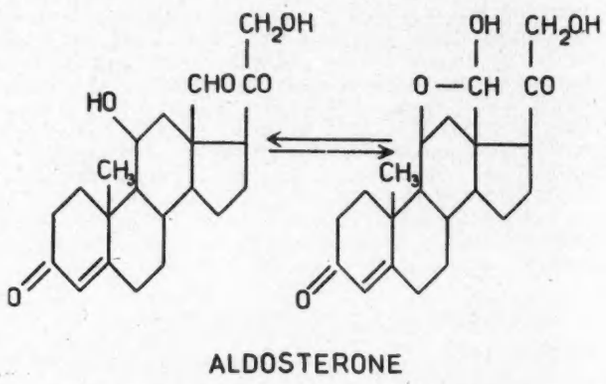
THE BEAUTIFUL WORK started in 1952 by Simpson and Tait,[1] who showed that a new steroid was responsible for the mineralocorticoid activity of the adrenals, culminated last year in the elaboration of its chemical formula by the same workers[2] in collaboration with Reichstein, Wettstein and their respective groups. Last July, Wettstein[3] announced its chemical synthesis. The discovery of this hormone, which illustrates so well the powers of modern organic chemistry and of the new research tools of radioactive isotopes and of paper chromatography, constitutes a landmark in the history of adrenal physiology and of the regulation of electrolytes in the human organism.

It is the purpose of this paper to review the present status of our knowledge about this hormone in clinical medicine. We will first describe its physiological action, then we will review the results of its therapeutic application, and finally we will summarize the results of studies on human subjects in normal as well as in pathological states.

The chemical formula of aldosterone (Fig. 1) shows that the important point which differentiates this hormone from cortisone, hydrocortisone and the other corticosteroids is the presence of an aldehyde group in position 18. In solution, aldosterone is mainly in the form of a hemiacetal between C_{11} and C_{18}. This hormone was originally isolated from beef adrenal extracts[1, 4] and was later identified in hog adrenal extracts,[5] and in adrenal venous blood of dogs[6, 7] and of monkeys.[5, 7] Luetscher, Neher and Wettstein[8] were able to prove the identity between this hormone and the sodium-retaining corticoid isolated from the urine of a nephrotic boy and which was apparently responsible in greater part for the sodium-retaining activity of crude urinary



ALDOSTERONE

Fig. 1.—Chemical structure of aldosterone.

extracts in œdematous states.[9] Recently, Wettstein[10] was able to isolate aldosterone from urine of patients with congestive heart failure, and we also were able to isolate it in pure form from the urine in a severe case of Cushing's syndrome.[11]

The comparative action of aldosterone, hydrocortisone and desoxycorticosterone is illustrated in Table I.

It is evident that aldosterone is much more potent than hydrocortisone in the regulation of electrolytes, whereas the latter is more active in the deposition of glycogen in the liver and in the production of eosinopenia. Selye[14] has recently demonstrated the prophlogistic activity of aldosterone, which antagonizes the activity of hydrocortisone in respect to the inflammatory reaction.

We must mention here the most interesting biosynthesis experiments of Wettstein, Kahnt and Neher[15] which suggest that desoxycorti-

TABLE I.

COMPARATIVE ACTION OF ALDOSTERONE, HYDROCORTISONE AND DOC (MODIFIED AFTER SAYERS[12])

	Aldosterone	*Hydrocortisone*	*DOC*
Liver glycogen deposition	25	100	1
Eosinopenia	0–50*	100	1
Life maintenance in optimal conditions	100		2.5
Resistance to cold stress	100	100	8
Na retention[13]	100	0.05	4
K excretion[13]	100	Retention	40
Fall in urinary Na/ratio[13]	100	8	17
Inflammatory response[14]	Enhancement	Suppression	

*Apparently, this variation is a function of the dose administered.

*From the Clinical Research Department, Hôtel-Dieu Hospital, Montreal.

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TABLE II.

STEROID BIOSYNTHESIS AFTER AEROBIC INCUBATION OF FRESH BEEF ADRENAL HOMOGENATES

*Supplements**	*ATP %*	*DOC %*	*Yield: µg/kg/adrenals*		
			Aldosterone	*F (Hydrocortisone)*	*B (Corticosterone)*
Suppl. and no incubation	0	0	61	230	630
No Suppl. + incubation	0	0	137	3,490	1,340
Suppl. + "	0	0	425	23,500	10,600
Suppl. + "	0.2	0	1,145	23,900	26,300
Suppl. + " (no nicotinamide)	0.2	0.05	*3,360*	3,760	53,000
Suppl. + incubation	0.002	0.05	2,410	22,560	80,400

*Nicotinamide 3 g./l.
Fumaric acid 4.64 g./l.
Glucose 18 g./l.
Salt solution.

Data from A. Wettstein

TABLE III.

ALDOSTERONE AND COMPOUNDS F, B, AND E IN NORMAL HUMANS

	Hydrocortisone (F)	*Corticosterone (B)*	*Cortisone (E)*	*Aldosterone*
Plasma concentration[16,17,18] (µg%)	7 - 11	4 - 8	3 - 4	0.05 - 0.08
Urinary excretion[19] (µg/day)	35 ± 7	0	91 ± 17	0.3 - 2 (?)

costerone could be a precursor of aldosterone. Experiments illustrative of this possibility are shown in Table II.

The relative plasma concentration of aldosterone, hydrocortisone, corticosterone and cortisone, and their respective urinary excretion, are indicated in Table III.

ADMINISTRATION OF ALDOSTERONE

The few milligrams which have been made available to several research groups throughout the world resulted in studies of the effect following administration of aldosterone to normal subjects, to patients with Addison's disease and to patients with rheumatoid arthritis. It is necessary here to remember that the data which will be summarized below come from studies resulting from the administration over periods of three to six days of a few milligrams. Thorn[20] gave one milligram of aldosterone intramuscularly each day for six days to a normal subject, and the following effects were observed (Table IV).

TABLE IV.

EFFECTS OF ALDOSTERONE IN NORMAL SUBJECTS

	1 mg. i.m. daily for 6 days (Thorn)
Urinary Na and Cl excretion	Fall
Urinary Na/K ratio	Fall
Urinary K	Increase
Eosinophils	No change: 300 µg; ↓ ↓ (1 mg.)
Urinary N	"
Urinary uric acid	"
17-Ketosteroids	"
17-OH-Corticoids	"
Serum lipids	"
Serum cholesterol	"
Glucose tolerance	"

Apart from the effect on electrolytes, no significant action was noted. Thorn[20] and Mach[21] have reported a marked fall in eosinophils in two normal subjects after a dose of one mg. This fall does not occur during continuous 12 hours' intravenous infusions of 100 micrograms of aldosterone[22] or intramuscular injections of 150 to 800 micrograms.[23, 24]

The administration of aldosterone in Addison's disease has been studied by Mach,[21, 23] Thorn,[20] Prunty,[24] Kekwick[25] and their co-workers. All these four groups have obtained fairly similar results (Table V).

The optimal dosage was found to be between 150 and 250 micrograms a day by intramuscular injection. The action of aldosterone is quite rapid, within 30 to 60 minutes. One interesting finding by Mach and Kekwick concerned the noticeable decrease in pigmentation occurring within six

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TABLE V.

ALDOSTERONE IN ADDISON'S DISEASE
(DOSAGE 150-250 MICROGRAMS A DAY)

	Increase	*Decrease*
Asthenia		– –
Exertional fatigue		– –
Skin pigmentation		? –
Urinary Na and Cl		– – –
" K	++	
" Na/K ratio		– – –
Serum K		– –
Salivary Na		– –
" K	+	
Weight	+	
Plasma volume	+	
N balance	0	0

days of treatment. This finding was not confirmed in the patient studied by Thorn.

The action of aldosterone on two patients with rheumatoid arthritis was studied by Ward[26] and co-workers at the Mayo Clinic. These patients received respectively 2.3 mg. and 4.7 mg. of aldosterone in six days. No change in the rheumatic activity was noticed. Apart from the usual sodium and chloride retention and a lowering in the potassium serum level, these authors did not observe any modification in blood eosinophils, in serum calcium, phosphorus, uric acid, urea, sugar or in blood pressure. Their findings strongly suggest that the presence of an hydroxyl group on C_{17} is essential for the anti-rheumatic activity of the corticosteroids.

STUDY OF ALDOSTERONE CONCENTRATION OR EXCRETION IN HUMANS

The study of urinary aldosterone in normal subjects as well as in patients with a variety of diseases has led to many interesting observations. Since there is a good deal of confusion,[27] we would like to insist on several points:

First, a distinction must be made between results as to sodium-retaining properties of crude urinary extracts and those of highly purified aldosterone obtained after two or more chromatographic separations of the crude extracts. At the Ciba Symposium on Hypertension in 1953 in London, we remarked that: "The bioassay for the estimation of urinary sodium-retaining factor will have its greatest value only if combined with a chromatographic separation of the substances contained in the crude lipid extracts of the urine".[28] The main reason for our assertion is that one probably does not get true observations unless the urinary extracts are purified (Venning).[29] We are in complete agreement with Tait, who does not think that there is any point in assaying crude extracts.[30] Therefore, when crude urinary extracts have been submitted for bioassay, we will speak only of the sodium-retaining activity of crude extracts of urine, whereas we will reserve the term "aldosterone equivalent in the urine" for aldosterone extracts which have been sufficiently purified by two or more chromatographic separations.

Second, some confusion and misinterpretation have arisen from the fact that several workers have expressed the results of determination of crude urinary extracts as micrograms of desoxycorticosterone or of aldosterone. This is not correct, in our opinion, since crude methylene chloride or chloroform extracts of urine contain a number of substances, some of which may provoke sodium retention and others sodium excretion, so that the end result is a summation of the effects of all these substances. It seems to us inappropriate to use a desoxycorticosterone or an aldosterone equivalent to express the total sodium-retaining effect of such crude extracts. Since, in addition, many results are based on assays of single doses (usually equivalent to 20 minutes' output of urine) it is debatable what quantitative weight can be given to such results.[31] Too often, there is no proper statistical analysis or indication of the fiducial limits.

Third, the sodium-retaining activity of crude extracts or the amounts of aldosterone or desoxycorticosterone equivalent vary greatly, depending on the hydrolysis-extraction procedure used. This point is far from being settled, and there is not, at the present time, any convincing evidence available.

The methods[13] we use in our laboratory for the extraction, hydrolysis, purification, isolation and determination of aldosterone are indicated in Tables VI and VII.

These methods are most complex and laborious. It takes a minimum of 5 to 6 weeks' work of a full-time technician to determine the aldosterone in a 24-hour urine of a single subject or patient. Progress in this field is greatly hampered by the lack of a specific and sufficiently sensitive chemical method to detect amounts of aldosterone of the order of 0.1 to 0.01 microgram.

TABLE VI.

ISOLATION OF URINARY ALDOSTERONE

1. Immediate extraction of a 24-hr. urine aliquot at pH 1.
2. Re-extraction after 24-hr. incubation at pH 4.5, 37°C., with β-glucuronidase (300 units/ml.).
3. Extract washings with N/10 NaOH (2) and with distilled water (1).
4. Isolation of the "aldosterone-cortisone fraction" by paper chromatography (toluene/propylene glycol).
5. Isolation of highly purified aldosterone after chromatographic separation of the "aldosterone-cortisone fraction" in Bush "C" system (toluene 90-ethyl acetate 10/50% methanol).

TABLE VII.

IDENTIFICATION AND DETERMINATION OF ALDOSTERONE

Physico-chemical procedure:
- Quantitative: Ultra-violet absorption at 240 millimicrons. Reduction of blue tetrazolium.
- Qualitative: RF values in different chromatographic systems. Absorption spectra in concentrated H_2SO_4 or in 100% H_3PO_4.

Bio-assay for Na-retaining substances:
- Day - 2 : Adaptation of 150-180 g. male rats to laboratory conditions.
- Day 0 : Bilateral adrenalectomy.
- Day 2 : Experiment:
  - 0 hour: Injection (0.1 ml.) of solvent (ETOH) or of aldosterone fraction. Ligature of urethra.
  - 4 hours: Total collection of bladder urine.
  - Indices of hormonal activity: Decreased Na excretion. Fall in Na/K ratio.
  - Expression of results: % of control group. Aldosterone equivalent with fiducial limits.

The factors which may possibly be involved in the secretion of aldosterone by the adrenal cortex are listed in Table VIII.

A great deal of work will be necessary to ascertain the respective value and importance, in different conditions, of each of the possible factors listed in the above table. Venning has found a definite increase in Na-retaining activity of crude urinary extracts in four out of five cases after intravenous infusions of growth hormone. In two normal adults on a diet restricted to 11 mEq. of sodium per day, Luetscher and Alexrad found a five-fold increase in urinary sodium-retaining substances per day compared with the control values.[36] These same authors[37] found that the urinary aldosterone excretion in children 4 to 8 years of age was about two-thirds of that in normal adults. They were unable to detect any sodium-retaining substances in the urinary extracts of Addisonian patients, or of two patients who had been previously submitted to bilateral adrenalectomy. They found an almost normal excretion of sodium-retaining substances in two patients with hypopituitarism.

TABLE VIII.

THE SUGGESTED FACTORS CONCERNED IN THE SECRETION OF ALDOSTERONE

1. Low Na diet.[32]
2. High K intake.[33]
3. Anxiety state—stresses.
4. Elevated venous pressure.
5. Variation in E.-C. fluid tonicity and volume (pitressin).[34]
6. Growth hormone.[35]

Luetscher and Johnson[38] found a very high sodium-retaining activity of crude urinary extracts obtained from children with the nephrotic syndrome. This sodium-retaining activity decreased when diuresis was produced by the use of ACTH, cortisone or concentrated salt-poor serum albumin.[39] Marked sodium-retaining activity in crude urinary extracts from most patients with congestive heart failure and almost all patients with cirrhosis of the liver was found by Luetscher and his co-workers[40] and by Singer and Wener,[41] Chart and Shipley[42] and Pechet and his co-workers.[43]

Conn[44] has recently described a syndrome which he has called primary aldosteronism, of which three other cases could be found in the literature. These analogous cases had been described as potassium-losing nephritis by Evans and Milne,[45] as potassium-depletion syndrome by Wyngaarden,[46] and as spontaneous hypopotassæmia by Mader and Iseri.[47] The clinical and biochemical description of these cases is given in Table IX.

Conn reported that no beneficial effect could be obtained from the administration of potassium salts. Two of these cases[44, 47] have been cured by

TABLE IX.

PRIMARY ALDOSTERONISM (CONN).

Clinical data:
- Intermittent tetany.
- Paræsthesiæ.
- Periodic severe weakness and "paralyses".
- Polyuria, polydipsia.
- Arterial hypertension.
- Lack of œdema.

Biochemical data:
- Serum pH = alkalosis > 7.55.
- Serum K = low 1.6 - 2.5 mEq/l.
- Serum Na = high.
- Sweat and salivary and urinary K = high.
- Sweat and salivary and urinary Na = low.
- High Na-retaining activity of urinary extracts.

Cause:
- Adrenocortical tumour or hyperplasia.

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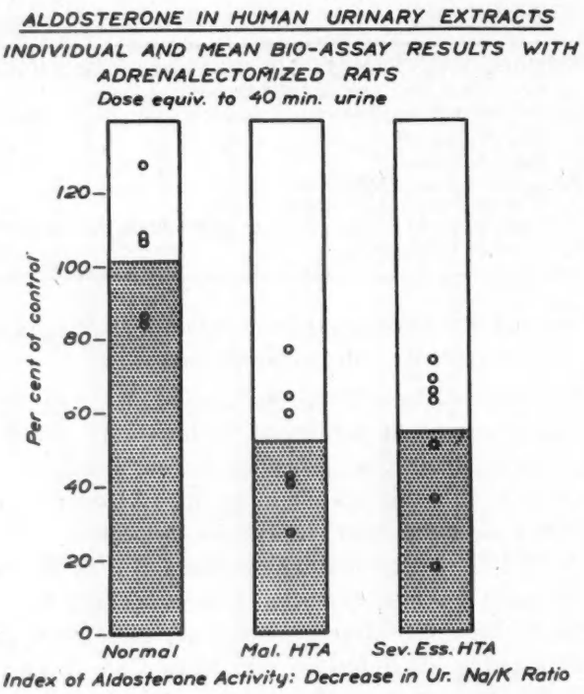

Fig. 2.—Results of aldosterone assay in normal subjects and in patients with malignant hypertension (Mal. HTA) and severe essential hypertension (Sev. Ess. HTA).
The individual results in normal subjects and hypertensive patients (indicated by the circles) and the mean results of each group (indicated by the dotted columns) are expressed as percentages of values in control groups of rats having received only the solvent used for injection of the aldosterone extract. The difference between 100% and the height of the columns representing the hypertensive groups is "proportional" to the quantity of aldosterone present. The importance of the difference between the normal and the two hypertensive groups is indicated by a t value of 4.85 ($p < 0.001$).

resection of the cortical tumour, and a third one[46] was found at autopsy to have adrenal glands weighing 20.5 g.—more than twice the normal weight of both adrenals. In Conn's patient the cortical adenoma was apparently made up chiefly of cells from the fasciculata zone.

Venning, Singer and Simpson[48] have found a marked increase in sodium-retaining activity of crude extracts in patients with toxæmia of pregnancy and with patients presenting a Cushing's syndrome. One patient with a very severe Cushing disease in the terminal stage was studied in our department. The main "mineralocorticoid" features of this patient were a serum potassium of 2.45 mEq./l., a serum sodium of 153 mEq./l. and blood pressure readings of 180-220/110-130 mm. Hg.

After plasma dialysis[49] aldosterone could be detected in peripheral blood by our bio-assay for sodium-retaining substances. The total plasma concentration, after dialysis and paper chromatographic separation,[49] was "1.12" microgram %, of which "0.65" microgram % was conjugated as glucuronide. It was isolated from the patient's urine in pure state, as evidenced by the RF values in three different chromatographic systems, ultraviolet absorption curve, blue tetrazolium reduction,[50] yellow fluorescence in caustic soda and the chromogen spectra in concentrated H_2SO_4[51] and in 100% H_3PO_4.[52] Its quantitative determination by ultraviolet absorption at 240 millimicrons and by the reduction of blue tetrazolium gave a 24-hour urinary excretion of 51.5 micrograms. Pure aldosterone was obtained, in this case, after five different chromatographic separations.[53]

Finally we would like to report the results of some of our work obtained in five normal adult males, six patients with malignant hypertension and seven with severe essential hypertension. The highly purified aldosterone fractions which were submitted for bioassay were obtained after the purification procedures described above.

The mean results and the dispersion of the individual values obtained with a dose of aldosterone extract equivalent to 40 minutes' secretion of urine are shown in Fig. 2. With the fall in urinary Na/K as the index of aldosterone activity, it is evident that a marked difference between the hypertensive groups and the normal subjects exists. The mean results obtained with aldosterone extract doses equal to 20 and 40 minutes' secretion of urine, as expressed by the decrease in sodium excretion and by the fall in the Na/K ratio, are shown in Fig. 3. With an extract equivalent to only 20 minutes' output of urine, the difference between the normal subjects and the two groups of hypertensive patients is not significant. However, a difference between the two groups becomes evident and very significant in tests using extracts corresponding to 40 minutes of urine output. The indices of aldosterone activity, decrease in sodium excretion and fall in Na/K ratio are quite concordant. Statistical analysis of the mean difference between normal subjects and hypertensive patients shows a t value of 4.85 ($p < 0.001$) for the urinary Na/K ratio and a t value of 3.27 ($p < 0.01$) for the Na retention index. The aldosterone equivalent (in micrograms per day) for each group of patients was calculated with fiducial limits at $P = 0.05$ (Table X).

These results suggest that the hypertensive patients secrete relatively larger amounts of aldosterone than normal subjects. This hyper-

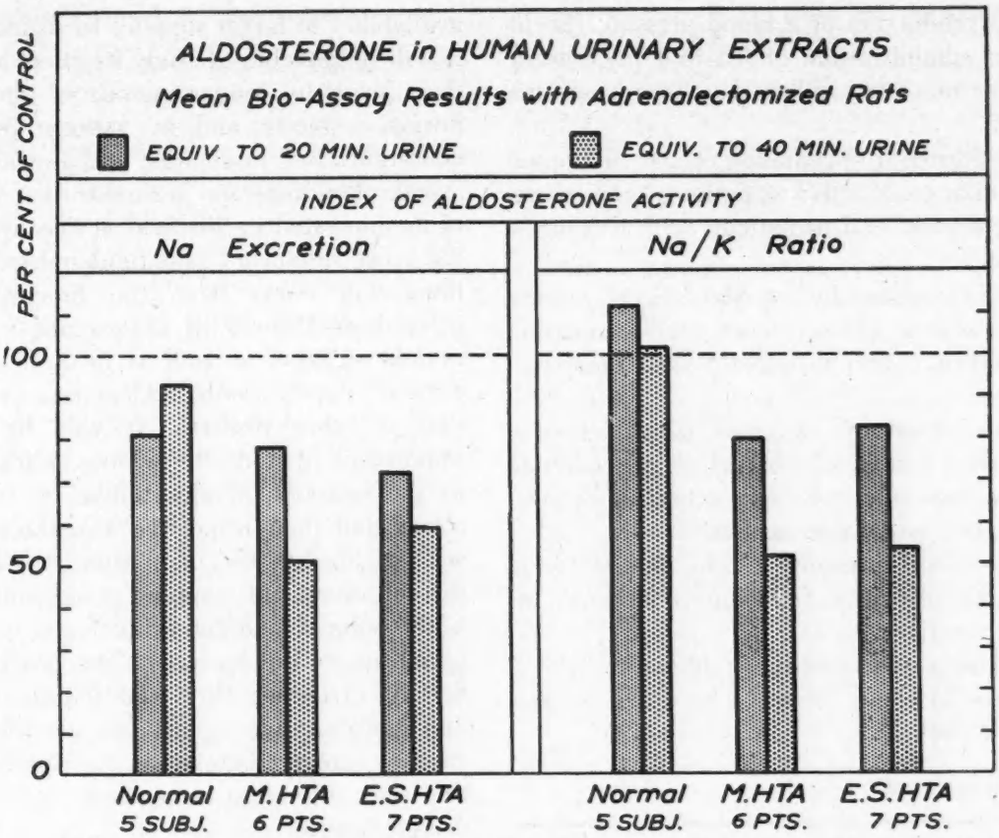

Fig. 3.—Mean bioassay results of highly purified aldosterone extracts from each group studied (*cf.* Fig. 2). All the results are expressed as percentages of control values, and the aldosterone activity is measured by the decrease in Na excretion and the fall in urinary Na/K ratio. The difference between the horizontal dotted line (100%) and the height of the columns is "proportional" to the amount of aldosterone present. The darker columns represent the mean results of the aldosterone extracts equivalent to 20 minutes' urine output whereas the lighter columns represent the dose equivalent to 40 minutes' urine.

aldosteronism may well be the missing link which could explain many clinical and experimental observations, such as the following:

1. The hypertension in Cushing's disease[54, 55] and the hypotension in Addison's disease.[56]

2. The hypertension in the primary aldosteronism syndrome of Conn.[44-47]

3. The correlation between the elevation of blood pressure in hypertensive patients and the sodium chloride intake.[57]

4. The beneficial effect in a certain number of hypertensive patients of the rice diet[58-60] or of diets limited to 250 mg. of sodium per day.[61-63]

5. The increased concentration of sodium in the muscles and arteries of patients with essential hypertension and of animals made hypertensive by various procedures.[64-66]

6. The hypertensive effect of desoxycorticosterone in normal subjects and in Addisonian patients receiving a diet "normal" in sodium.[67-70] The potentiating effect of salt on the DOC pressor activity[71, 72] and the disappearance of this effect when salt is withdrawn from the diet.[72, 73] This hypertensive effect is increased in animals in which renal functional mass has been reduced.[74] The same effect has been noted in nephritic and in hypertensive patients after desoxycorticosterone administration.[70, 75]

TABLE X.

URINARY ALDOSTERONE AND HUMAN ARTERIAL HYPERTENSION

Malignant hypertension	*μg./day*	*Fiducial limits at P=0.05*	*μg./40 min.*
(*6 patients*)			
Na-retention.....	7.2	3.74 - 13.75	0.2
Fall in Na/K....	5.47	2.19 - 13.94	0.152
Severe essential hypertension (*7 patients*)			
Na-retention.....	7.82	3.52 - 17.12	0.217
Fall in Na/K....	8.45	4.48 - 15.89	0.235

7. The rise in blood pressure following an increase in dietary salt in hypertensive patients[72] and the disturbance in salt and water excretion following salt restriction.[76]

8. The production of a blood pressure rise in rats after administration of 0.5 to 1 microgram of aldosterone every other day during several weeks.[77]

9. The identical appearance of the capillaries of the bulbar conjunctiva in patients with essential hypertension and in patients with Cushing's syndrome.[78]

10. The hypertrophy of the adrenal cortex (mainly the zona glomerulosa) after angiotonin administration,[79] and in experimental renal hypertension.[80]

11. The significant decrease of the hypertension after complete removal of the adrenal cortex in dogs and rats with acute or chronic experimental renal hypertension.[81-83]

12. The blood pressure fall in patients with essential hypertension following restriction of dietary potassium.[84]

In summary, the clinical conditions in which aldosterone has been found to be increased are listed in Table XI.

TABLE XI.

HYPERALDOSTERONISM

Normal subjects on low-sodium diet. Pathological states having in common:
A—*Generalized œdema*
Nephrotic syndrome
Cirrhosis of the liver
Congestive heart failure
B—*Persistent elevation of blood pressure*
Toxæmia of pregnancy
Cushing's syndrome
Primary aldosteronism
Essential hypertension
Malignant hypertension

It is of interest to note that there are two main clinical conditions in which aldosterone is increased: (1) where the common factor is generalized œdema; (2) where there is a persistent rise in blood pressure. In the former group, aldosterone is more likely an effect than a cause, whereas in the latter group it would be, according to the evidence available, directly involved in the causation and pathogenesis of the condition.*

Now that the chemical synthesis of aldosterone has been achieved and that we can foresee the availability of larger supplies for clinical studies, it will be possible to study its effect at different dose levels for longer periods of time, both in normal subjects and in various pathological conditions. But, fascinating and appealing as this aspect of aldosterone administration is to those of us interested in this field, it may well be that the most significant and fundamental contributions will come from the biochemical and physiological study of aldosterone secretion in normal subjects as well as in diseases such as arterial hypertension, œdematous states and various other diseases. It will be of great importance to study the various factors involved in the secretion of aldosterone by the adrenal cortex and their respective importance. But, as we said earlier, the main stumbling-blocks are the laborious and complex procedures involved in the isolation and determination of infinitesimal quantities of this hormone. The progress in this field is extremely slow and requires the work and collaborative efforts of several workers. Already, great progress has been made, and we feel that still more is to come in the not too distant future.

*It is interesting to speculate at this point if the hyperaldosteronism observed in human arterial hypertension could be caused by a high potassium intake combined or not with repeated anxiety stresses, the pressor effect being possibly potentiated by a normal or a high sodium intake. Work along this line is in progress in our Department.

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REFERENCES

1. TAIT, J. F., SIMPSON, S. A. AND GRUNDY, H. M.: *Lancet*, 1: 122, 1952.
2. SIMPSON, S. A. *et al.: Helvet. chim. acta*, 37: 1200, 1954.
3. SCHMIDLIN, J. *et al.: Experientia*, Sept. 15, 1955.
4. MATTOX V. R., MASON, H. L. AND ALBERT, A.: *Proc. Staff Meet. Mayo Clin.*, 28: 569, 1953.
5. GRUNDY, H. M. *et al.: Acta endocrinol.*, 11: 199, 1952.
6. FARRELL, G. *et al.: Proc. Soc. Exper. Biol. & Med.*, 87: 141, 1954.
7. SIMPSON, S. A., TAIT, J. F. AND BUSH, I. E.: *Lancet*, 2: 226, 1952.
8. LUETSCHER, J. A., NEHER, R. AND WETTSTEIN, A.: *Experientia*, 10: 456, 1954.
9. DEMING, Q. B. AND LUETSCHER, J. A.: *Proc. Soc. Exper. Biol. & Med.*, 73: 171, 1950.
10. WETTSTEIN, A.: Personal communication.
11. NOWACZYNSKI, W. *et al.:* To be published.
12. SAYERS, G.: Proc. 6th Annual Conf. on the Nephrotic Syndrome. Nat. Nephrosis Found., New York, 1954, p. 202.
13. GENEST, J. *et al.:* In Symposium on Aldosterone, Proc. Montreal Physiological Soc., Montreal, 1955.
14. SELYE, H.: *Science*, 121: 368, 1955.
15. WETTSTEIN, A., KAHNT, F. W. AND NEHER, R.: *Ciba Found. Coll. Endocrinol.*, 8: 170, 1955.
16. SIMPSON, S. A. AND TAIT, J. F.: *Ibid.*, 8: 204, 1955.
17. MORRIS, C. J. O. R. AND WILLIAMS, D. C.: *Bioch. J.*, 54: 470, 1953.
18. *Idem: Ciba Found. Coll. Endocrinol.*, 7: 267, 1954.
19. DECOURCY, C. *et al.: J. Endocrinol.* 9: 401, 1953.
20. THORN, G. W. *et al.: Ann. New York Acad Sc.*, 61: 609, 1955.
21. MACH, R. S. AND FABRE, J.: *Ciba Found. Coll. Endocrinol.*, 8: 361, 1955.
22. LEMIEUX, G., DAVIGNON, A. AND GENEST, J.: *Canad. M. A. J.*, in press.

23. MACH, R. S. *et al.: Schweiz. med. Wchnschr.*, **84**: 407, 1954.
24. PRUNTY, F. T. G. *et al.: Lancet*, **2**: 620, 1954.
25. KEKWICK, A. AND PAWAN, G. L. S.: *Lancet*, **2**: 161, 1954.
26. WARD, L. E. *et al.: Proc. Staff Meet. Mayo Clin.*, **29**: 649, 1954.
27. GENEST, J.: Editorial, *Canad. M. A. J.*, **73**: 221, 1955.
28. *Idem:* Ciba Found. Symp. on Hypertension, Little, Brown & Company, Boston, 1954.
29. VENNING, E. *Ciba Found. Coll. Endocrinol.*, **8**: 201, 1955.
30. TAIT, J. F.: *Ibid.*, **8**: 201, 1955.
31. COPE, C. L.: *Ibid.*, **8**: 201, 1955.
32. LUETSCHER, J. A. AND AXELRAD, B. J.: *Proc. Soc. Exper. Biol. & Med.*, **87**: 650, 1954.
33. LARAGH, J. H. AND STOERK, H. C.: *J. Clin Invest.*, **34**: 913, 1955.
34. BECK, J. C. *et al.:* 68th Annual. Meeting, Ass. Am. Phys., 1955.
35. VENNING, E.: *Ciba Found. Coll. Endocrinol.*, **8**: 190, 1955.
36. AXELRAD, B. J. AND LUETSCHER, J. A.: *J. Clin Invest.*, **33**: 916, 1954.
37. LUETSCHER, J. A. AND AXELRAD, B. J.: *J. Clin. Endocrinol.*, **14**: 1086, 1954.
38. LUETSCHER, J. A. AND JOHNSON, B. B.: *J. Clin. Invest.*, **33**: 276, 1954.
39. AXELRAD, J., JOHNSON, B. B. AND LUETSCHER, J. A.: *J. Clin. Endocrinol.*, **14**: 783, 1954.
40. LUETSCHER, J. A. AND JOHNSON, B. B.: *J. Clin. Invest.*, **23**: 1441, 1954.
41. SINGER, B. AND WENER, J.: *Am. Heart J.*, **45**: 795, 1953.
42. CHART, J. J. AND SHIPLEY, E. S.: *J. Clin. Invest.*, **32**: 560, 1953.
43. PECHET, M. M. *et al.: Ibid.*, **33**: 956, 1954.
44. CONN, J. W.: *J. Lab. & Clin. Med.*, **45**: 6, 1955.
45. EVANS, B. M. AND MILNE, M. D.: *Brit. M. J.*, **2**: 1067, 1954.
46. WYNGAARDEN, J. B., KEITEL, H. G. AND ISSELBACHER, J.: *New England J. Med.*, **250**: 597, 1954.
47. MADER, I. J. AND ISERI, L. T.: *J. Lab. & Clin. Med.*, **44**: 895, 1954.
48. VENNING, E. H., SINGER, B. AND SIMPSON, G. A.: *Am. J. Obstet. & Gynec.*, **67**: 542, 1954.
49. NOWACZYNSKI, W. AND GENEST, J.: *J. Clin. Endocrinol.*, in press.
50. NOWACZYNSKI, W., GOLDNER, M. AND GENEST, J.: *J. Lab. & Clin. Med.*, **45**: 818, 1955.
51. ZAFFARONI, A.: *J. Am. Chem. Soc.*, **72**: 3828, 1950.
52. NOWACZYNSKI, W. AND STEYERMARK, P.: *Arch. Biochem.*, in press.
53. NOWACZYNSKI, W. *et al.:* To be published.
54. COPE, O. AND RAKER, J. W.: *New England J. Med.*, **253**: 119 and 165, 1955.
55. SOFFER, L. J. *et al.: Ciba Found. Coll. Endocrinol.*, **8**: 487, 1955.
56. THORN, G. W.: The Diagnosis and Treatment of Adrenal Insufficiency, Am. Lecture Series, No. 29, Charles C Thomas, Springfield, Ill., 1949.
57. DAHL, L. K. AND LOVE, R. A.: *Fed. Proc.*, **13**: 426, 1954.
58. KEMPNER, W.: *North Carolina M. J.*, **5**: 125 and 273, 1944.
59. *Idem: Am. J. Med.*, **4**: 545, 1948.
60. *Idem: Ann. Int. Med.*, **31**: 821, 1949.
61. AMBARD, L. AND BEAUJARD, E.: *Semaine Méd.*, **25**: 133, 1905.
62. WATKIN, D. W. *et al.: Am. J. Med.*, **9**: 441, 1950.
63. DOLE, V. P. *et al.: J. Clin. Invest.*, **29**: 1189, 1950.
64. TOBIAN, L. AND BINION, J. T.: *Ibid.*, **32**: 608, 1953.
65. *Idem: Circulation*, **5**: 574, 1952.
66. TOBIAN, L.: Abstracts 47th Ann. Meet. Am. Soc. Clin. Invest., Atlantic City, 1955.
67. PERERA, G. W. *et al.: J. A. M. A.*, **125**: 1030, 1944.
68. FERREBEE, J. W. *et al.: Ibid.*, **113**: 1725, 1939.
69. THORN, G. W. AND FIROR, W. M.: *Ibid.*, **114**: 2517, 1940.
70. PERERA, G. A. AND BLOOD, D. W.: *Ann. Int. Med.*, **27**: 401, 1947.
71. KNOWLTON, A. T. *et al.: J. Exper. Med.*, **85**: 187, 1947.
72. PERERA, G. A. AND BLOOD, D. W.: *J. Clin. Invest.*, **26**: 1109, 1947.
73. GENEST, J.: *Union méd. Canada*, **80**: 11, 1951.
74. SELYE, M., HALL, C. E. AND RANLEY, E. M.: *Canad. M. A. J.*, **49**: 88, 1943.
75. THORN, G. W. *et al.: Ann. Int. Med.*, **37**: 972, 1952.
76. PERERA, G. A. AND BLOOD, D. W.: *Am. J. Med.*, **1**: 602, 1946.
77. GORNALL, A. G.: Personal communication.
78. LEE, R. E.: *Am. J. Med.*, **19**: 203, 1955.
79. DEAN, H. W. AND MASSON, G. M. C.: *J. Clin. Endocrinol.*, **11**: 193, 1951.
80. RATHER, L. J.: *Stanford M. Bull.*, **8**: 119, 1950.
81. GOLDBLATT, H.: *Ann. Int. Med.*, **11**: 69, 1937.
82. PAGE, I. H.: *Am. J. Physiol.*, **122**: 352, 1938.
83. COLLINS, D. A. AND WOOD, E. H.: *Ibid.*, **123**: 224, 1938.
84. PERERA, G. A.: *J. Clin. Invest.*, **32**: 633, 1953.

CONGENITAL CYSTS AND FISTULÆ OF THE NECK*

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MUCH HAS BEEN WRITTEN about cysts and fistulæ of the neck, but there is still much controversy regarding the pathogenesis of these lesions; in spite of the fact that the management of such abnormalities has been remarkably well outlined by various authors, we still see cysts that have been incised and drained or inadequately removed. It is for these reasons that I am presenting a few cases I have had the opportunity of observing in the last year or so.

Congenital cysts and fistulæ of the neck may be divided into the midline or thyroglossal, and the lateral or so-called branchial cysts and fistulæ.

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MIDLINE OR THYROGLOSSAL CYSTS AND FISTULÆ

The midline cysts and fistulæ are fairly well accepted as arising from the thyroglossal duct. During the development of the human embryo the isthmus of the thyroid gland is derived from a bud of hypoblast which arises in the midventral portion of the floor of the pharynx. This bud migrates downward, forming the thyroglossal duct. Epithelial rests anywhere along the course of this tract may give rise to a cyst or a fistula. The fistula usually reaches the exterior following infection of a cyst by breaking through the thin skin lining. It is very exceptional to see a midline fistula at birth; ordinarily they are secondary, resulting from infection of a cyst.

Wenglowski does not believe in the thyroglossal tract theory, and states that these cysts and fistulæ always end in a blind sac at the level of the hyoid bone to which they may be firmly attached. He further states that the tract between the hyoid bone and the foramen cæcum is never

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patent. In one case we shall see histological evidence of a sinus leading into the foramen cæcum, and in another case clinical evidence of patency of the duct.

A thyroglossal cyst may develop anywhere from the foramen cæcum to the suprasternal notch. In 92 cases Bailey records three beneath the foramen cæcum; six in the floor of the mouth protruding beneath the chin; 12 in the suprahyoid region; 37 in the subhyoid region; 23 on the thyroid cartilage or membrane, and four in the suprasternal notch. They are far more frequent in the infrahyoid regions. We are taught that thyroglossal cysts are exactly in the midline but we occasionally see them off-centre, particularly those found at the level of the thyroid cartilage, which by its configuration more or less pushes the cyst to one side.

Thyroglossal cysts are more frequently observed in children, but may develop at any age. Both sexes appear to be equally affected. The clinical picture is that of a midline "lump or bump," which may vary in size from a few millimetres to four or five centimetres. It is not adherent to the overlying tissues but moves in a vertical direction on swallowing. Forced protrusion of the tongue also moves the cyst, a sign distinguishing it from a dermoid cyst, which does not move. The picture may be complicated by infection which very often will result in a fistula.

LATERAL OR SO-CALLED BRANCHIAL CYSTS AND FISTULÆ

If authors are in reasonable agreement regarding the pathogenesis of the midline cysts and fistulæ, this is not so in the case of the laterally placed ones.

Two distinct theories prevail. The first and oldest maintains that lateral cysts and fistulæ develop primarily from the branchial apparatus, particularly from the second and the third pouches. The second theory, formulated by Wenglowski and interpreted by Meyer, who reviewed this question in 1932, explains these abnormalities as arising from epithelial rests of the pharyngo-thymic duct.

Arguments for and against every theory have been formulated, and it would be beyond the scope of this paper to go into this controversial subject. For the moment all that can be said is that this question still remains to be clarified.

Unlike the midline fistulæ, the lateral fistula is frequently present at birth. Many, however, are acquired as a result of either an infection or an ill-advised incision of a cyst. At birth the true fistula may consist of only a small dimple and remain as such for a number of years before starting to discharge. The discharge is usually serous until infection sets in, when it becomes purulent and causes irritation of the surrounding skin. The sinus opening is located along the anterior border of the sternomastoid muscle, anywhere from the ear above to the clavicle below. One can sometimes feel the sinus tract as a small subcutaneous cord running up along the anterior border of the muscle.

The cyst is usually seen below the angle of the mandible, in front of or beneath the sternomastoid muscle. It develops at any age but is more common in the third decade, and presents itself as a slowly growing nontender mass. The growth may be so slow as to reach a considerable size before being noted by the patient. The cyst very often develops after an infection of the throat or surgical procedure on the throat such as tonsillectomy. Pain is an exceptional symptom unless there is an infection. Pressure upon surrounding structures may, in time, give rise to certain symptoms such as cough through irritation of the vagus nerve.

Some authors have reported that congenital cysts and fistulæ are more frequently observed in the female sex, but a review of the reported cases indicates that males are probably affected as frequently as females.

Fistulæ are divided into three groups: the complete fistula extending from the pharynx, usually the tonsillar fossa, to the outside; the external fistula having only an external opening; and the internal fistula opening into the pharynx only. This last group is rare. Semken states that one-third of the fistulæ are complete.

There seems to be a definite familial tendency to these congenital abnormalities and it is not infrequent to see in the same patient preauricular fistulæ. Our two patients had bilateral cervical and pre-auricular fistulæ.

PATHOLOGY

Thyroglossal cysts and fistulæ are lined by either a stratified squamous or a ciliated columnar cell epithelium. Mild lymphocytic and plasma cell infiltration are usually seen, and

chronic inflammatory changes are noted where infection has occurred.

Lateral cysts and fistulæ, on the other hand, present a far more interesting histological picture which is characteristic of these conditions.

The cyst wall is thin, and interiorly presents small ridges suggesting lobulation. The epithelium, which may be either stratified squamous or ciliated columnar cell, is infiltrated by lymphocytes, forming a veritable lympho-epithelial symbiosis exactly comparable to that found in the tonsil. It is thus easy to understand the term "kyste amygdaloide", used to describe these cysts in the French literature. Underlying the epithelium is a lymphoid tissue base with germinal follicules.

DIAGNOSIS

The history and complete and careful examination of the patient will help in making the correct diagnosis of congenital cyst or fistula, which should not be confused with the following: dermoid cysts, cystic hygroma, lipoma, tuberculous adenitis, hæmangioma, deep cervical abscesses, the various mycoses, carotid body tumour, adenopathies and metastatic carcinoma.

TREATMENT

The use of sclerosing agents recommended by some authors is mentioned only to be condemned. The treatment of these abnormalities is surgical and requires complete and careful excision of the lesion. For thyroglossal tract anomalies the excision must include the midportion of the hyoid bone and a core of tissue from the hyoid bone up to the foramen cæcum, as described by Sistrunk. For lateral cysts, complete excision by careful dissection through a wide exposure is recommended in order to avoid injury to surrounding structures. Lateral fistulæ must be followed up to the end. In cases of complete fistula, some authors recommend inverting the stump into the pharynx, but this does not appear to be necessary. The stepladder incision described by Bailey is most useful, otherwise one finds oneself working in a deep hole.

CASE 1.—G.B., a 9-year-old boy, was seen in August 1953 because of a discharging sinus in the midline of the neck. The history dated back six years, at which time a small lump, present for some time, had spontaneously ruptured. Since then the sinus had discharged a serous liquid, increasing in amount at meal times and causing irritation of the surrounding skin.

On examination a small pinpoint fistula was seen in the midline about 1 cm. below the level of the hyoid bone. The skin surrounding the fistula was reddened and fissured. After his admission to hospital, operation was deferred a few days because of dermatitis of the face. On October 6 the fistulous tract was excised according to Sistrunk's technique. The postoperative course was essentially uneventful.

Pathology.—Microscopically the specimen consisted of an elliptical piece of skin, in the middle of which could be seen the orifice of the fistula, the fistulous tract leading to a piece of hyoid bone, and muscle tissue in which no tract could be made out. Microscopically a sinus tract lined with ciliated columnar epithelium was seen. There was slight lymphocytic and plasma cell infiltration. A section made in the muscle tissue beyond the hyoid bone showed the fistulous tract surrounded by muscle.

This shows the importance of removing the hyoid and core of tissue extending to the foramen cæcum; the operation is otherwise not complete and recurrence is certain.

CASE 2.—G.B., a 48-year-old man, was first seen in June 1953 because of a midline mass in his neck, present for years and variable in size. On examination a large 2 x 2 cm. mass was noted at the level of the thyroid cartilage. The skin overlying this mass was somewhat tense and adherent. The mass moved upwards on swallowing. Pressure exerted upon the mass brought forth a thick discharge which was seen to ooze through the foramen cæcum. This manœuvre had been performed repeatedly by the patient in order to reduce the size of the mass. Operation, recommended on several occasions, was again refused in spite of the warnings of the possibility of infection. In September 1953 the patient finally decided to have the cyst removed, and arrangements were made for his admission to the hospital. However, two weeks later he returned to the office complaining of pain and an increase in size of the mass, which had become red and tender to touch. The cyst had become infected. High doses of antibiotics were immediately ordered but these failed to prevent fistulization. Finally the infection subsided to a certain extent and on November 12 the cyst was excised. The operation, which necessarily had to include a large section of overlying skin, was not without difficulty as considerable inflammatory reaction had taken place, and the cyst was found to be adherent to the thyroid gland. Contrary to practice in other cases, a drain was left in place for a couple of days because of the recent infection. The postoperative course, however, was uneventful.

Pathology.—A ciliated columnar epithelium lined the cyst cavity and tract. Areas of ulceration were seen throughout. A very marked chronic inflammatory cell reaction was seen underlying the epithelium.

CASE 3.—C.B., a 29-year-old woman, consulted me in June 1953 because of a lump in the middle of the neck. The lump, first noted two years previously, had gradually increased in size. Examination showed a small midline mass measuring approximately 1 x 1 cm. just below the level of the hyoid bone.

Operation, performed on November 19, revealed a cystic mass which by dissection was found to extend up and somewhat to the left of the midline over the hyoid bone. At this point we wondered whether it really was a thyroglossal cyst, but on pushing up of the dissection the mass suddenly popped out after separating some fibres of the mylohyoid muscle through which it extended.

Pathology.—This turned out to be an epidermoid cyst lined by a squamous cell epithelium.

This case is included because it presented itself as a thyroglossal cyst and demonstrates that sometimes correct diagnosis may be made only at operation.

CASE 4.—M.G., a man 34 years of age, was seen in November 1953 because of a slowly growing mass on the left side of his neck. The mass was first noted by the patient two months previously. There was no pain or pressure symptoms. On examination a large 4 x 4 cm. mass was felt on the left side of the neck below the angle of the mandible and partly covered by the sternomastoid muscle. Operation on November 14 revealed a large cystic mass lying over the thyrolingual trunk. The postoperative course was normal.

Pathology.—The cyst contained a thick greyish discharge. Its thin wall was lined with squamous cell epithelium in which numerous lymphocytes were scattered. Beneath the epithelium lay a lymphoid tissue chorium with germinal centres. The lympho-epithelial symbiosis characteristic of these congenital cysts and fistulæ was well demonstrated.

CASE 5.—J.P.A., a 3½-year-old boy, was referred in October 1952 because of discharging cervical sinus since birth, repeated sore throat and nasal obstruction. On examination bilateral preauricular fistulæ were noted, the right one being scarred after repeated incisions and drainage. The left fistula was a mere dimple and had never discharged. Adenoids and large infected tonsils were present. Small discharging sinuses were noted on each side of the neck, in front of the sternomastoid muscle at the level of the thyroid cartilage. The surrounding skin was excoriated.

On October 27 the tonsils and adenoids were removed and the right preauricular fistula was excised. The child was then allowed home with instructions to return in one month for excision of the cervical sinuses. The sinuses were excised at two sittings on November 25 and 27 using the stepladder incision. Both sinuses were found to extend to the pharynx without opening into it, and passed between the two carotids. The postoperative course was uneventful.

Pathology.—Sections of the fistula revealed a columnar epithelium with lymphocytic infiltration, overlying a lymphoid tissue base.

CASE 6.—T.M., a 21-year-old man, gave a history of discharging cervical sinuses since birth. His mother also presented the same anomaly. On examination, bilateral preauricular and cervical fistulæ were noted. The cervical fistulæ were somewhat lower than the level of the thyroid cartilage. A considerable skin reaction due to the continuous discharge surrounded the sinus opening. At operation on June 13, the findings were similar to those in Case 5. This patient later died from nephritis.

SUMMARY

A brief review of congenital cysts and fistulæ of the neck is made without any attempt to explain their pathogenesis. The importance of correct diagnosis and proper management, which is by total excision, is stressed.

Six cases are presented particularly to demonstrate certain histological features.

It is believed that these conditions belong in the field of otolaryngology and should be treated by the otolaryngologist. This is logical for he is better acquainted with the embryology and anatomy of this region. Furthermore, only he is capable of properly examining the different cavities of the head and neck, an examination which is so important to eliminate a possible focus or primary tumour whenever dealing with lumps in the neck.

REFERENCES

1. BAILEY, H.: *Brit. J. Surg.*, **21**: 173, 1933.
2. *Idem*: *Brit. J. Surg.*, **12**: 579, 1925.
3. BLASSINGAME, C.: *Ann. Otol., Rhin & Laryng.*, **56**: 395. 1947.
4. DUBREUIL, G.: *Embryologie Humaine*, Vigot Frères, Paris, 1929.
5. HALL, C.: *Laryngoscope*, **60**: 368, 1950.
6. MALCOLM, R. B. AND BENSON, R. E.: *Surgery*, **7**: 187, 1940.
7. MCLAUGHLIN, C. W., JR.: *Arch. Surg.*, **57**: 450, 1948.
8. MEYER, H. W.: *Ann. Surg.*, **59**: 1, 226, 1932.
9. NEEL, H. B. AND PEMBERTON, J. de J.: *Surgery*, **18**: 267, 1945.
10. LAHEY, F. H. AND NELSON, H. F.: *Ann. Surg.*, **113**: 508. 1941.
11. SISTRUNK, W. E.: *Ann. Surg.*, **71**: 121, 1920.

Case Reports

LEPTOSPIROSIS SEJROE*
WITH REPORT OF A CASE

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IN RECENT YEARS increased attention has been drawn to human leptospiral infection in North America. Before 1938 only infection with *L. icterohæmorrhagiæ* had been reported. In that year, Meyer, Eddie and Anderson-Stewart described the first case of canicola fever[1] and other reports followed.[2 etc.] More recently there have been reports of *L. pomona*,[3, 4] *L. grippotyphosa*[5] and *L. bataviæ*[6] infections. Then the organism of Fort Bragg fever, after 10 years of passage through laboratory animal hosts, was identified as *L. autumnalis*.[7] *L. ballum* and serotypes of the *pyrogenes* and *hebdomadis* groups have been reported in man from Puerto Rico.[8, 9, 10]

In Canada, several cases of Weil's disease due to *L. icterohæmorrhagiæ* have been described,[11, 12, 13] but no other leptospiral infections

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were reported until 1955 when Saint-Martin reported a case of canicola fever with meningitis.[14]

Although agglutinations against the organism have been observed in livestock herds in the U.S.A., particularly in Florida,[10] the following is thought to be the first instance of human infection with *Leptospira sejroe* reported in North America.

The patient was a 39-year-old bank manager residing in a lakeshore suburb near Montreal. He was quite well until September 27, 1954, when he developed a headache, anorexia and pains in his joints. That night he suffered from bad dreams and continued to do so on succeeding nights.

On September 28 he suffered from pains in both knees and called his physician, who found fever (102° F.) and throat redness. The patient also pointed out a skin lesion remaining from a dog bite suffered two weeks before on the right index finger. He complained of a slightly tender lump in the right axilla. The physician noted red streaks up the right arm. Neither local lesion nor streaks were very tender. The patient was given 900,000 units of penicillin intramuscularly.

On September 29, the patient seemed somewhat better, and was given 600,000 units of penicillin. That day he developed severe headache and photophobia and was quite confused during the night. On September 30, he was admitted to Queen Mary Veterans' Hospital at 10.45 a.m.

On September 12, the patient had been bitten by his 1½-year-old cocker spaniel. There was merely a superficial abrasion on the right index finger, which healed at first but then developed a vesicle just before the generalized illness began. In hospital the lesion presented as an indolent ulcer with slight remaining vesiculation.

The dog had been ill repeatedly since acquired by the patient 1½ years previously. About every four months he suffered from diarrhœa, with blood and mucus in his stools. He had been seen by several veterinarians who had diagnosed various conditions, including hepatitis. He had been treated shortly before the bite with an injection for an illness similar to the others.

When the patient's illness began, he decided that the dog should be destroyed, and this was arranged on Oct. 2. Unfortunately this was done before samples of the dog's serum or urine had been obtained. Furthermore, the dog had been dead for some time before the patient's physicians were notified and it was then thought too late for necropsy to be of any value.

The patient kept a garden, but it was not damp or swampy and not many mice had been observed about it. The dog had not been seen catching mice.

Condition on admission (Sept. 30, fourth day of illness).—Temperature was 98.2° F., rising in the afternoon to 99.8°, but subsiding then to 99° or lower for two days. Pulse rate was 95; blood pressure was 110/70 mm. Hg. Physical examination was negative except for the right hand and arm; there was a small partly healed but slightly moist lesion on the dorsum of the right index finger, with a small vesicle at its proximal end. Streaks of lymphangitis were seen running up the forearm and arm and over the lateral aspect of the right chest. A hard gland the size of a plum was felt in the right axilla. There was tenderness but not the marked tenderness of pyogenic adenitis. He was complaining of constant headache and had periods of mental confusion. There was moderate photophobia. No retinal or conjunctival changes were noted.

Course: He was started on rather small doses of antibiotics, 300,000 units of penicillin and 0.5 g. streptomycin, each twice daily. On this medication his temperature seemed well controlled, but he still suffered from mental confusion at night. On Oct. 3, he complained of severe headache and in the afternoon the temperature rose to 102° F. There was no definite neck rigidity, but Kernig's sign was moderately positive.

Lumbar puncture was done on Oct. 4. Pressure was 280 mm. H_2O; fluid was clear and flowed freely. There were 234 neutrophils and 416 monocytes per cu. mm. The level of total proteins was 94 mg. %, sugar 76 mg. % and chlorides 679 mg. % (as NaCl). Dark-field examination of the spinal fluid revealed no spirochætes.

Antibiotic dosage was increased on Oct. 4 to crystalline penicillin, one million units every three hours, and streptomycin, 0.5 g. twice a day. At the same time triple sulphonamides were started. From this time the temperature fell, the symptoms abated and mental confusion ceased. The penicillin was continued till Oct. 10 (total 45,400,000 units in hospital), the streptomycin and sulphonamides till Oct. 8. He was discharged quite well on Oct. 10, and returned to work on Nov. 1. From Dec. 5 to 17 and occasionally subsequently he suffered from vertigo. He was seen for this in the neurology clinic on Dec. 21. Neurological examination was negative and the condition was thought to be a postural vertigo. Otherwise, he has had no significant illness to date (May 1955).

Other Laboratory Data: Cultures of blood, urine, C.S.F. and a swab of the lesion on the right index finger all yielded no growth of bacteria, leptospira or other organisms. The cultures were put up on routine media; the C.S.F. was also cultured on Fildes' medium and cysteine agar.

Dark-field examinations of blood, C.S.F., urine and material from finger lesion and also stained smears were all negative.

Animal inoculation (guinea pig, rabbit and mouse): blood smears, tissue cultures and animal autopsy material were all negative.

Urinalysis: Negative on admission. Developed 17 mg. % of albumin on Oct. 3, with 15 to 20 white cells, occasional red cells and rare small granular casts. Albumin level rose to 37 mg. % on Oct. 4, but no albumin or casts were found on Oct. 6 or thereafter.

Hæmogram: Sept. 30: white cells 7,700; differential: neutrophils 88% (mature cells 78%, young cells 10%, immature cells 0%), lymphocytes 9%, monocytes 3%; hæmoglobin 14.7 g. %.

Oct. 4: white cells 11,100; differential: neutrophils 77% (mature cells 75%, young cells 2%, immature cells 0%), lymphocytes 17%, monocytes 6%; hæmoglobin 12.9 g. %; erythrocyte sedimentation rate 92 (Westergren).

Oct. 12: white cells 6,800 (N. 64%, L. 35%, E. 1%); Hb. 14.2 g. %; E.S.R. 23.

Serology: VDRL exclusion test negative.

C.S.F. Wassermann: anti-complementary.

Blood Chemistry: Oct. 4: blood urea 18.1 mg. %, bilirubin 0.5 mg. %; cephalin cholesterol flocculation negative. Oct. 5: glucose (AC) 86 mg. %, (PC) 176 mg. %. Oct. 12: blood urea 13.3 mg. %; bilirubin 0.5 mg. %, bromsulphalein test: 2.4% of dye retention in ½ hour.

Agglutinations.—Serum samples were submitted to Dr. R. D. Stuart, Professor of Bacteriology at the University of Alberta, who kindly performed the leptospiral agglutinations. Each serum was tested against the following leptospiral sero-types: *autumnalis, ballum, bataviæ, bovis, canicola, grippo-typhosa, hebdomadis, hyos, icterohæmorrhagiæ, pomona, pyrogenes and saxkœbing.*

On Oct. 4, 1954, the serum titre to *L. sejroe* was 1/300 (weak 1/1,000), on Oct. 12, 1/1,000, on Oct. 19, 1/300, and on May 19, 1955, 1/10 (trace 1/30). Low titre cross-agglutinations (1/10 to 1/100) to *L. grippo-typhosa, L. hebdomadis* and *L. bovis* were demonstrated in certain of these sera, but in each case *L. sejroe* seemed to be the only significant agglutination.

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DISCUSSION

Leptospira sejroe was recognized as a separate type by Borg-Petersen and Christensen in Denmark.[15-17] In 1936-37 some indications were given that there might be a new type from serological reactions on routine specimens.[18] Finally, in November 1937, a new type of leptospira was isolated from the blood of a young fisherman, on the little island of Sejroe near Seeland, who was suffering from an acute illness characterized by sudden onset of fever, headache, vomiting, muscular pains, herpes labialis, mental disturbances and slightly increased C.S.F. pressure, but no increase in cells. The spirochætes showed cross-agglutinations with other strains, notably *L. hebdomadis*, but differed to a certain extent from all of them, so that it was considered a distinct strain and was named after the island on which the first patient resided.

Borg-Petersen and Christensen described 10 cases in 1939, in one of which there were jaundice and severe neurological effects; this case was also reported separately by Mortensen.[19] In 1949 Borg-Petersen reported 414 cases diagnosed at the State Serum Institute in Copenhagen.[18] Nielsen and Hertel described 29 cases seen in Denmark from 1937 to 1943 with particular attention to clinical detail.[20]

These reports tend to group cases as "leptospirosis sejroe" although some appeared to be due to *L. saxkœbing*, a closely allied type described by Borg-Petersen in 1944; still others appeared to be due to infection with a third strain whose status has not been clearly established.

Mino described the disease in Italy[21] and Babudieri has written at length about leptospirosis in the Italian rice fields, some of it due to *L. sejroe*.[22] Other reports have been received from Germany, Czechoslovakia, Switzerland[23, 24] and Yugoslavia.[25] Buckland and Stuart reported a case in a British soldier in N.W. Europe.[26] As noted previously, the presence of animal infection in the U.S.A. has been suggested by agglutination reactions.[10]

The disease occurs about equally among males and females. It is rare below the age of 14. The onset is sudden with high fever (104° to 104.8° F.) lasting 9 to 10 days. Headache occurs in all cases and is typically aggravated by sitting up. Vomiting, shivering fits, myalgia and injection of episcleral vessels occur in 50% of cases or more. Mental slowing and amnesia are common. Meningeal symptoms were seen in 25% of Nielsen and Hertel's cases. Five of their cases showed pathological changes in the cerebrospinal fluid with a rise in albumin, globulin and cells, chiefly lymphocytes. They describe two cases with disturbances of cardiac rhythm doubtfully due to specific effects of the disease. Redness of the fauces and exanthems of varying type have been described. Jaundice was observed in 56 (13.5%) of 414 cases of *L. sejroe* and similar infections recorded in Denmark up to 1948.[18] Peripheral nerve lesions occurred in 25% of Nielsen and Hertel's cases. Two of these patients, one being also reported by Mortensen, suffered from paralysis of the lower limbs.[19, 20]

There is no typical white cell count. The sedimentation rate is usually elevated. Albuminuria is common, and in some cases red blood cells and granular casts are found.

Leptospira have been isolated from the blood in a small proportion of cases from the second to seventh days of illness. In a few cases the organisms have been found in the urine about the 21st day of disease. Serological reactions develop about the beginning of the second week. Agglutination of leptospira by the patient's serum usually occurs to a titre of 1/300, but in some cases to 1/1,000.

The disease usually runs a benign course but deaths have been reported. Borg-Petersen reported three deaths (0.7%) in the 414 cases of the *sejroe* group up to 1948.[18] Babudieri implies that the disease is more severe in Italy than in Denmark and that fatal cases sometimes occur.[21]

The main reservoir of the infection in Denmark is the harvest mouse *(Mus musculus spicilegus)*. It is also found in the woodmouse *(Apodemus sylvaticus)*. Petersen found the organism in the kidneys of a mouse from a farm where a human case of *L. sejroe* had occurred. Case incidence in humans shows a rise in August for males and in September for females. This is presumably because the males become infected in the fields at harvest time; the mice then follow the crops to the barns, and hence the later occurrence of cases among females.[18] Practically all cases occur among the rural population.

Besides occurring in mice, the disease has been found in swine, horses and cattle.[23] Steigner[27] reports the case of a sick dog with a positive agglutination for *L. sejroe*. The dog de-

veloped nephritis and died. Necropsy was refused.

Infection usually occurs indirectly. The animal carrier excretes leptospira in the urine, this contaminating mud or water. The organisms then enter the human body through the skin or mucous membranes. Usually infection occurs through abrasions, but entry can take place through intact skin if it is softened by prolonged soaking. Infection may also occur from the saliva of an infected dog.[22]

In the present case, no proof of etiology was obtained by smear or culture of leptospira from either the patient or an animal source of infection. It is possible that no growth was obtained in the cultures from the patient because of a suppressive effect of antibiotics. However, the typical clinical course and the agglutination reactions give reasonable grounds for the diagnosis. Circumstantial evidence tends to incriminate the dog as the source of infection. The dog, in turn, probably acquired the infection in some way from a murine source. This leads to the conclusion that *L. sejroe* and other lesser known leptospira infect their usual hosts in Canada as in other countries. It is also possible that some cases of undiagnosed fever and "aseptic" meningitis in human subjects may be due to leptospiral infections. Consideration of this diagnosis by attending physicians may lead to confirmation by culture or agglutination.

TREATMENT

Most of the studies on treatment of the leptospiroses have been in reference to *L. icterohæmorrhagiæ*. In the earlier years arsenic, bismuth and sulphonamides were used with little effect. Abroad, antisera were used but there were great practical difficulties caused by delay in type diagnosis. Patterson in Hawaii[28] found that transfusions of blood from recovered cases had a prompt effect.

Several scattered reports have appeared to indicate efficiency of penicillin and other antibiotics. Bulmer,[29] Patterson,[28] and Suchett-Kaye[30] all reported the efficacy of penicillin if given early in the disease. In Reid and Reed's case[13] improvement seemed to follow institution of penicillin therapy; streptomycin was used in the latter part of the disease. There have been reports also of an apparent effect from chlortetracycline[31, 32] and oxytetracycline.[33]

Meyer and Brunner[34] discuss effects of antibiotics in dogs. They conclude that penicillin is effective in the first week of disease, but fails to eradicate the organisms after they have become established in the renal tubules. Streptomycin is also effective in the early stages. They investigated treatment of the carrier state with streptomycin and considered it effective.

On the other hand, in a survey based on 67 cases of infection with various leptospira in Puerto Rico, Hall *et al.*[35] studied the effect of five antibiotics and concluded that none was particularly effective. However, their daily dose of penicillin was 550,000 units and the mean total dosage was 6.5 million units. In the present case of *L. sejroe*, at such dosage levels the disease was not controlled; but improvement seemed immediate when the dose was increased to eight million units daily. The interpretation of this response is complicated by the coincidental administration of streptomycin and sulphonamides, either of which may have had some effect in controlling the infection.

SUMMARY

1. A case is reported of fever, meningitis, mental disturbances and mild transient nephritis.

2. Immunological reactions suggest that the condition was due to infection with *Leptospira sejroe*.

3. Circumstantial evidence suggests that the infection was contracted through a dog bite.

4. The history, clinical nature and geographical incidence of the disease are reviewed. This is thought to be the first human case in North America.

5. The disease appeared uncontrolled by lower dosages of penicillin but improvement seemed to begin when the dose was increased to eight million units daily.

6. It is suggested that some cases in Canada of fever or meningitis of doubtful etiology may be caused by the lesser known leptospira.

Thanks are expressed to Dr. Hugh Starkey, Chief of Laboratory Services, Queen Mary Veterans' Hospital, and to Professor R. D. Stuart of the University of Alberta, both of whom reviewed the early draft of this report and offered valuable suggestions. Dr. Starkey was the first to suggest the possibility of a spirochætal infection causing the patient's fever.

REFERENCES

1. MEYER, K. F., EDDIE, B. AND ANDERSON-STEWART, B.: *Proc. Soc. Exper. Biol. & Med.*, 38: 17, 1938.
2. ROSENBAUM, H. D.: *Arch. Int. Med.*, 78: 531, 1946.
3. BEESON, P. B., HANKEY, D. D. AND COOPER, C. F. Jr.: *J. A. M. A.*, 145: 229, 1951.

4. SCHAEFFER, M.: *J. Clin. Invest.*, **30**: 670, 1951.
5. SPAIN, R. S. AND HOWARD, G. T.: *J. A. M. A.*, **150**: 1010, 1952.
6. GOCHENOUR, W. S. Jr. *et al.*: *Fed. Proc.*, **10**: 408, 1951.
7. *Idem*: *Pub. Health Rep.*, **67**: 811, 1952.
8. YAGER, R. H. AND GOCHENOUR, W. S. Jr.: *Am. J. Trop. Med.*, **1**: 457, 1952.
9. GOCHENOUR, W. S. Jr. AND YAGER, R. H.: *Proc. Am. Vet. M.A.*, p. 178, 1952.
10. GLEISER, C. A.: Personal communication from American Army Medical Service Graduate School.
11. BATES, J. E.: *Canad. M. A. J.*, **16**: 1466, 1926.
12. BLANCHARD, A. J. AND JAIMET, C. H.: *Ibid.*, **43**: 19, 1940.
13. REID, E. A. S. AND REED, R. W.: *Ibid.*, **63**: 479, 1950.
14. SAINT-MARTIN, M. AND CHARBONNEAU, J. H.: *Ibid.*, **73**: 454, 1955.
15. BORG-PETERSEN, C.: *Acta Convent tertii de trop. atque malar. morbis*, **1**: 396, 1938.
16. BORG-PETERSEN, C. AND CHRISTENSEN, H. I.: *Compt. rend. Soc. de biol.*, **130**: 1507, 1939.
17. BORG-PETERSEN, C.: *Ugest. læger*, **101**: 679, 1939.
18. ALSTON, J. M. *et al.*: *Proc. Roy. Soc. Med.*, **42**: 707, 1949.
19. MORTENSEN, V.: *Compt. rend. Soc. de biol.*, **130**: 1510, 1939.
20. NIELSEN, O. P. AND HERTEL, E.: *Acta med. scandinav.*, **70**: 384, 1945.
21. MINO, P.: *München. med. Wchnschr.*, **88**: 96, 1941. Abstr. *Bull. Hyg.*, **16**: 637, 1941.
22. BABUDIERI, B.: *WHO Monograph Series*, **19**: 117, 1953.
23. GSELL, O.: *Ergebn. inn. Med. u. Kinderh.*, **1**: 367, 1949.
24. FREY, W.: *Schweiz. med. Wchnschr.*, **78**: 531, 1948. Abstr. *Bull. Hyg.*, **23**: 684, 1948.
25. FALISEVAC, J.: *Arhiv. Hig. Rada. Zagreb*, **2**: 159, 1951. Abstr. *Bull. Hyg.*, **27**: 158, 1952.
26. BUCKLAND, F. E. AND STUART, R. D.: *Lancet*, **2**: 331, 1945.
27. STEIGNER, K. F.: *Zentralbl. Bakt., Abt. 1*, **156**: 216, 1950.
28. PATTERSON, H. M.: *J. A. M. A.*, **134**: 1007, 1947.
29. BULMER, E.: *Brit. M. J.*, **1**: 113, 1945.
30. SUCHETT-KAYE, A. I.: *Lancet*, **1**: 90, 1951.
31. BRAINERD, H. D. *et al.*: *J. Clin. Invest.*, **28**: 992, 1949.
32. BATCHELOR, T. M. AND TODD, G. M.: *J. A. M. A.*, **143**: 21, 1950.
33. LIEBOWITZ, D. AND SCHWARTZ, H.: *Ibid.*, **147**: 122, 1951.
34. MEYER, K. F. AND BRUNNER, K. T.: *Acta Tropica, Basle*, **7**: 1, 1950. Abstr. *Bull. Hyg.* **25**: 921, 1950.
35. HALL, H. E. *et al.*: *Ann. Int. Med.*, **35**: 981, 1951.

MASSIVE NECROSIS OF THE LIVER DUE TO TRICHLORETHYLENE*

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TRICHLORETHYLENE is widely used in industry as a degreasing fluid, dry-cleaning agent and solvent. It has largely replaced other chlorinated hydrocarbons previously used for these purposes, such as carbon tetrachloride and tetrachlorethane, because it is much less toxic.

The most marked effects of trichlorethylene are on the nervous system, and indeed it is widely used as an anæsthetic. Industrial poisoning has resulted in giddiness, ataxia, cranial nerve palsies, polyneuritis, loss of consciousness and death due to respiratory failure, cardiac arrest or ventricular fibrillation. Several standard textbooks and monographs state that trichlorethylene is not toxic to the liver.[1-5] However, a search of the literature reveals that death due to massive hepatic necrosis has been produced by this agent.[6-13] The purpose of this report is to emphasize the danger of liver damage from trichlorethylene by presenting the case of a man who died of massive hepatic necrosis following exposure to this solvent.

E.F., male, age 37, consulted one of us (G.W.H.) on August 7, 1954. He had felt tired for several months but since Aug. 1 his fatigue had increased considerably and in addition he had nausea and loss of appetite. The patient was a chemist in a plant where trichlorethylene was used as a solvent. On July 31, he had supervised the preparation of the solvent mixture and had been exposed to trichlorethylene vapour for a period of 2½ hours. He stated further that he had always previously worn a mask for this work, but on July 31 he could not find a filter for his mask and so carried on without it.

He was a thin man with a slight icteric tint to his scleræ. The blood pressure was 90/70 mm. Hg. The liver was not enlarged or tender. There were no abnormal neurological signs and the rest of the physical examination was negative. Admission to hospital was recommended.

When he was admitted on August 10, the jaundice had increased but the physical findings were unchanged. The fasting blood sugar (87 mg. per 100 ml.), blood urea nitrogen (14 mg. per 100 ml.) and serum alkaline phosphatase (7 units) were normal. Serum bilirubin was 2.4 mg. per 100 ml. and the cephalin flocculation reaction was strongly positive. The urine specific gravity was 1.019, there was no albumin or glucose, and microscopic examination did not reveal any cells or casts. A diagnosis of toxic hepatitis due to trichlorethylene was made and he was given a high carbohydrate, high protein diet, supplemented by intravenous glucose.

During the next four weeks the jaundice increased and his general condition became worse. On August 28, spider nævi and ascites were noted. On September 2, he became confused and lapsed into coma. He was now deeply jaundiced and died three days later. His temperature had been normal throughout but rose to 100.2° F on the last day.

The prominent post-mortem finding was acute massive necrosis of the liver. The liver weighed only 1,070 grams. The left lobe was almost totally necrotic but the right lobe was much less involved. There was no productive fibrosis. Additional findings were ascites, bilateral pleural effusion, acute pulmonary congestion and biliary nephrosis.

There is no doubt that this patient was exposed to trichlorethylene. He spent most of his working time performing analytical assays of pulp and paper. This did not involve the use of chlorinated hydrocarbons or other liver poisons. Contact with trichlorethylene occurred during the preparation of a solution used for processing paper, 1000 lb. of trichlorethylene being piped

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into an open tank to which were added paraffin and a smaller amount of synthetic resin. The mixture was stirred mechanically. When the solids were completely dissolved, the solution was piped into a closed storage tank. The whole process took about 2½ hours. During the mixing operation workmen wore masks with activated charcoal filters. The patient claimed that he had always worn his mask except for one occasion on July 31, the day before he became seriously ill. The patient had supervised this process at least once every two to three weeks for the past year and a half. There was no forced ventilation in this room, which was also used for the recovery of trichlorethylene from solution after application to paper.

Later analyses of samples of air from this room before and during the preparation of a batch of solution gave the following concentrations of trichlorethylene in parts per million:

Operating area, before batch (doors and windows closed)	37	p.p.m.
	134	"
	188	"
Operating area, during batch (doors and windows closed)	188	"
	200	"
	297	"
Near mixing tanks, during batch (doors and windows opened)	200	"
	184	"
	37	"

SUMMARY

A case of massive necrosis of the liver following industrial exposure to trichlorethylene is presented. Attention is drawn to the fact that trichlorethylene may cause liver damage, notwithstanding the generally accepted view that it is non-toxic to the liver.

We are grateful to Dr. Donald Hunter for helpful suggestions in the investigation of this case.

REFERENCES

1. STÜBER, K.: *Arch. F. Gewerbepath. u. Gewerbehyg.*, 2: 398, 1931.
2. VON OETTINGEN, W. F.: *J. Indust. Hyg.*, 19: 349, 1937.
3. HUNTER, D.: Industrial Toxicology, Oxford University Press, New York, 1944.
4. OSTLERE, G.: Trichlorethylene Anæsthesia, E. and S. Livingstone, Edinburgh, 1953.
5. BROWNING, E.: Toxic Solvents, Edward Arnold and Co., London, 1953.
6. CARRIE, P. A., PERRAULT, M. AND BOURDIN, J. S.: *Arch. mal. profess.*, 3: 345, 1941.
7. GERMAIN, A. AND MARTY, J.: *Bull. et mem. Soc. méd. hôp. Paris*, 63: 1044, 1947.
8. DEROBERT, L. *et al.*: *Ann. méd. lég.*, 32: 28, 1952.
9. KLEINFELD, M. AND TABERSHAW, I. R.: *A. M. A. Arch. Indust. Hyg.*, 10: 134, 1954.
10. DODDS, G. H.: *Brit. M. J.*, 1: 769, 1945.
11. HERDMAN, K. N.: *Ibid.*, 2: 689, 1945.
12. Annotation: *Lancet*, 1: 379, 1944.
13. Annotation: *Ibid.*, 1: 476, 1944.

Special Article

A GLIMPSE OF NEUROPHYSIOLOGY IN THE SOVIET UNION*

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[*Editor's Note: Dr. Penfield was asked to set down his impressions of his recent visit to the Soviet Union. In reply he says, "I am sending you these notes. You will find them fragmentary, but I hope they are accurate as far as they go." He has also included the names and addresses of the directors of the various institutions he visited to make exchange of information possible. The "notes" Dr. Penfield has so kindly contributed open up a vista of an immense amount of fascinating research, whose existence must have been unknown to the majority of our readers.*]

DURING my two weeks' stay in the U.S.S.R. I was the guest speaker of the Academy of Sciences and was treated with unfailing courtesy and hospitality. I was welcomed first at mid-morning tea, in the Presidium of the Academy, by the General Scientific Secretary, Academician Topchiev, and a distinguished group of neurophysiologists. After that, the time was filled with lectures and as many visits to institutes as the time would allow, with sightseeing and amusement added.

Since my visits were chiefly to the centres of neurophysiology and I spoke usually as a clinical physiologist, I shall make no attempt to discuss clinical medicine in any detail in this letter but refer largely to neurophysiology.‡

The addresses were made easy and agreeable for me by the fact that Professor G. D. Smirnov, who is himself a neurophysiologist working in one of the Academy's laboratories on the ganglionic activity of the retina, acted as my interpreter (both for efferent and afferent streams of communication!). He even undertook, at times, to explain the speaker's point of view on his own initiative.

The major interest in the long discussions that followed each address turned on the relationship of cortical stimulation to the work of the Pavlov School and on the problem of centrencephalic integration of cortical function in the two hemispheres. I think it is no exaggeration to say that these audiences were at least as familiar with our writings on the subject as the average audience would have been in any English-speaking community.¶

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†Director of the Montreal Neurological Institute.
‡The visits to these institutes were, of necessity, rapid and if I have failed at times to grasp the full significance of the work demonstrated, I offer my apologies to the investigators who gave me such a warm welcome on each occasion.
¶In Leningrad a member of the audience startled me by asking how the patient K.M. was getting along! Fortunately, I recalled the case of K.M. which I published, with

There are many neurophysiological institutes in Moscow and Leningrad. Some are organized and supported by the Academy of Sciences, others by the Academy of Medical Sciences, rather than by the universities or medical schools.

Western physicians will understand the present situation better if, before describing these institutes, I refer at once to the "Scientific Session on the Physiological Teachings of Academician I. P. Pavlov" conducted by the U.S.S.R. Academy of Sciences, in common with the Academy of Medical Sciences in 1950. The session attracted much public notice, in the Soviet Union and abroad. It was translated into English by the Academy and published at least in part.

Fig. 1.—Ivan Petrovich Pavlov. After a painting by Nesterov.

The discussion opened with a quotation from Stalin's message in regard to linguistics: "It is generally recognized," he wrote, "that no science can develop and flourish without a battle of opinions, without freedom of criticism." All scientists everywhere must applaud such a statement.

But what followed came as a surprise to most of us since the introductory statement referred to opposition to the theories of Pavlov in "the bourgeois countries". It is common knowledge in the West that our physiologists, including Sherrington and his followers, have been unanimous in their recognition of the importance of Pavlov's work.*

I am discussing this session frankly because scientists outside the Soviet Union have wondered about its outcome. Many were under the impression that a trial had been staged rather than a free discussion. This was apparently a misconception, for no penalties were imposed. Some physiologists were accused of a defect in their loyalty to "Pavlov's materialist teachings", or as being influenced by the "dualist and animist" point of view, or of worshipping "foreign science and cosmopolitanism".

I can testify to the fact that all of these physiologists, involved in this discussion five years ago, are continuing to carry on constructive scientific work, without interruption and with no lack of facilities.

Moscow

1. INSTITUTE OF NORMAL AND PATHOLOGICAL PHYSIOLOGY, ACADEMY OF MEDICINE† DIRECTOR: V. N. TCHERNIGOVSKY

Professor Tchernigovsky came to Moscow from Leningrad three years ago to take charge of this institute, succeeding Razenkov in this position.

Professor Donald Hebb, in 1940, under the title—"Human Behaviour after Extensive Bilateral Removal from the Frontal Lobes." I replied that K.M. was well and working full time, but that he proved to be irresponsible, shifting about from job to job. When I added that possibly they had known workmen like that in the U.S.S.R., even without operation, there was a general laugh.

*Lashley has pointed out that it was the "philosophers" who were unwilling to accept the conditioned reflex theory as the final basis for a physiological explanation of behaviour, and so limited the impact of the work that gave Pavlov "his greatest claim to genius." See the discussion of the influence of Pavlov's conditioned reflex work on psychology (Pavlov, A Biography. B. P. Babkin, University of Chicago Press, 1949, pp. 319-322).

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It is a large, well-equipped institution with 130 investigators and a total staff of 300. Speransky is the chief of a laboratory of pathology here. The work is subdivided and carried out in a large number of semi-autonomous laboratories.

In the Director's room was a copy of a magnificent painting (Fig. 1) by the Russian artist, Nesterov, which shows Pavlov with his arms outstretched and his fists clenched on a kymograph tracing that lies across the desk before him. The gesture is obviously one of impatience. Through the window beyond the desk could be seen the laboratories and the countryside of Koltushi, sometimes called the "Capitol of the Conditioned Reflex". I was told that he had made this gesture when demanding of the artist how long he expected him to sit idle.

Tchernigovsky is a quiet, forceful director with a comprehensive understanding of the work of his associates. The over-all project to which the institute is devoted is the "study of the nervous regulation of different functional processes, normal and pathological". There are two major divisions, one of physiology and the other of experimental pathology. The projects include conditioned reflex studies, comparative neurology, metabolism, experimental therapy, electrophysiology, endocrinology, and invention of new apparatus.

In some laboratories, Pavlov's work on the digestive system of animals is being repeated, using visceral movement as the indicator of tract activity instead of secretory changes alone. Another project is to make a thoroughgoing study of the physiology of the alimentary system after gastrectomy.

The long corridors of Tchernigovsky's Institute were lined by padded doors, made soundproof for the benefit of the workers in the laboratories. Patient, well-nourished dogs stood in a long succession of rooms and Pavlov chambers, with different types of pouches dripping from fistulous openings out of the alimentary tract.

In the histological laboratory, Dr. E. Pletchkova demonstrated enormous increase in the size of the *boutons terminaux* on the cells of the spinal cord, in Clarke's column, after crushing the sciatic nerve. This hypertrophy of the synapses, she said, was similar to that reported by Doinkov, in 1911, in cases of multiple sclerosis.

2. Institute of Highest Nervous Activity of the Academy of Sciences*
Director: Professor Ivanov Smolensky

This large research institute was organized five years ago in the temporary quarters of an old palace. A new building is now nearing completion to receive it.

*Address: Pjatnizkaia, 48, Moscow.

"Highest nervous activity" is a broader term than "conditioned reflex" and was preferred by Pavlov during his latter years. As the name suggests, the major interest in this Institute seems to be focused on the conditioned reflex as a phenomenon rather than on the function of the nervous system as a whole.

Attention is directed toward the establishment and recording of conditioned reflexes in animals and man, using motor responses to a signal, as well as visceral or vegetative responses.

In man when speech, hand movement and vegetative responses were studied following the conditioned stimulus of sound of a certain duration, the vegetative response, such as the galvanic skin reflex recorded from the palm of the hand, was found to be more accurate than response by hand movement or words.

Thus, the involuntary response was more accurate than the so-called voluntary. Differences in duration of the auditory stimulus which were not detected when the human subject was waiting to respond by word or movement were detected accurately by the involuntary response.

Professor Kutlarewsky is chief of the department of experimental pathology in this institute. In his department the effects of intoxication by drugs or infection are studied using animals of various species which have been conditioned or are in the process of being conditioned.

Dr. Alexandrovskaya, a woman histologist, demonstrated in excellent histological preparations the enlargement of mitochondria that occurs in nerve cells as the result of infection.

3. Physiology Laboratory of the Academy of Sciences*
Chief: Professor A. A. Asratyan

Asratyan is an enthusiastic physiologist of Armenian descent who was a pupil of Pavlov for 10 years. He takes justifiable pride in his own ability as an experimental neurosurgeon, and in the significance of the long series of experiments. His spirit was reflected in the keenness of his assistants. And even the dogs, responding to good care and kindness, seemed to be anxious to help.†

The first problem in this laboratory had to do with what Asratyan called the functional plasticity of the nervous system. For 20 years he has studied restoration of function following what may be called mutilating operations such as the crossing of nerves, amputation of limbs, removal

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†High consideration of the dog is a good Pavlovian tradition. In Leningrad there is a large statue of the laboratory dog, inspired by Pavlov. At the top is a magnificent hound done in bronze and below, around the base of the statue, are small carvings of laboratory scenes. An operation is shown in one panel. In another, a dog is seen licking the incision on the neck of its mate. And tributes are added to the dog as the best friend of man.

of cerebellum, removal of labyrinths, incisions in spinal cord or medulla.

After experiments upon a thousand animals and removal of cerebral cortex in a hundred, during experiments that have extended over the years, he concludes that restoration of function depends upon the cerebral cortex.*

In adult animals, function that returned after lesions were made, disappeared again after removal of the cortex of one side but the animal learns to compensate again in time. After the removal of cortex on the second side the restored function disappears, never to return again.

As an example, let the vagus nerve be anastomosed to the right median nerve, or the spinal cord be cut on the right side. Function in the right leg will return in time. Then removal of cortex on the left side will bring back the early disability (more markedly than ipsilateral corticectomy). But function does return again in time. Later removal of the remaining cortex however causes it to be lost again, never to return.

He demonstrated an animal which had learned to walk after removal of the cerebellum but had lost that restored ability when the cerebral cortex was excised on both sides. The animal was very active, lying on the floor and moving all limbs well. He was willing to fight or to eat at appropriate times, but was unable to walk.

The conclusion was that adaptive restoration of function, and compensation for injury, is due to the cerebral cortex. This, he said, bears out the ancient dictum of Pavlov that the "cortex is chief".

But this conclusion holds true for adults only and for higher animals only. The young dog or the lower animal is capable of securing restored function to a considerable degree when only the subcortical structures remain intact.

The second problem studied by Asratyan's group had to do with the role of the cortex in regard to unconditioned reflexes, for example the response of salivation to the appearance of food. This response decreases as the result of ipsilateral corticectomy. After operation the response becomes the same for all kinds of food, whereas before corticectomy the salivation was greater for meat than it was for bread.

Many other unconditioned reflexes are decreased or abolished as follows: after removal of one cortex, and more so after bilateral removal, the blood pressure adjustment is seriously defective. After removal of one cortex, the withdrawal of 2% of the total blood of the animal causes a serious drop in the pressure and after the bilateral operation blood loss to the extent of only 1% may result in death. The erythropoietic function is gravely altered; the function of the reticulo-endothelial system is defective as shown by the slow disappearance of congo red from the system; the leukocytic reactions are altered.

But hormonal reactions are increased. The animals become adrenaline-sensitive and the oxygen demand at rest is increased four times.

The third major problem in this laboratory is the study of "highest nervous activity" or conditioned reflexes. They have five well-equipped Pavlov chambers. Asratyan has found that, in completely soundproof chambers, dogs go to sleep and so his chambers are only partially soundproof, but equipped with excellent recording devices.

Dr. Sahiulina hammers tiny metal spikes, insulated except at the tip, through the scalp into the skull of the dog for purposes of electroencephalography. This is done, as I observed, without discomfort to the dog, and no infection has resulted.

When the dogs were studied in Pavlov chambers, she found a great increase in cortical electrographic activity as the result of unconditional stimulation. This occurs in both hemispheres.

She recorded the movement of animals' legs by means of lights attached to the legs and projected on a record called a "cyclogram". Or the dog stood on a "stabilograph" which recorded weight and movement of all four paws by points of recorded light. Excellent records were secured of many of these things on ink-writers.

The general conclusions are that unconditioned reflexes, as well as conditioned reflexes, are dependent upon the cerebral cortex for their organization. Furthermore, the restoration of function after injury to the nervous system (peripheral or central) depends upon the cortex, particularly the contralateral cortex for limb function, and the ipsilateral cortex for the salivary glands.

Finally, it is of interest to neurosurgeons that strong views are held in this laboratory regarding postoperative treatment, views that were also originally inspired by Pavlov. Sleep, Asratyan states, without deep narcosis restores function. It overcomes the "inhibition" that arrests function in the postoperative period.

They are in the habit of giving calcium chloride and sedative drugs, such as urethane and bromide, with sufficient discrimination to produce sleep without coma.

4. INSTITUTE OF NEUROLOGY OF THE ACADEMY OF MEDICAL SCIENCES*

DIRECTOR—ACADEMICIAN KOINIVALOV

During the war this institute was connected with the Second Medical Institute under the direction of Professor Propper-Graschenko. It is housed in an ancient building and contains 86

*All this is summarized in his book entitled *The Physiology of the Central Nervous System*. Published by the Academy of Sciences, Moscow, 1953.

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neurological beds but provides for no neurosurgical treatment.

Interesting work was in progress on human myography by Dr. Philippe Bassin and his woman associate, Dr. Usevitch. When myographic recording of the index finger was carried out they observed an increase in myographic activity, if the subject was told to prepare for movement without making a movement. There was, of course, further increase when the hand was moved.

In another experiment, a curved plastic strip was hung on the lower lip so as to record from electrodes on the inner side of the lip. Simultaneous record was made from the index finger. When the subject was given a problem in arithmetic, or was presented with the problem of wrongly spelled words, there was increased activity within the lip, although there was no movement of the lip, while there was no increase in the finger myogram.

When an aphasic patient was made the subject of this experiment, there was greatly increased activity in the lips if he or she was asked to formulate words without speaking, while there was no corresponding change in the finger myogram. On the other hand a patient who was mute, as the result of hysteria, showed no increase in electrical activity in the lip myogram but did show a marked increase in the finger when she or he was asked to formulate words in the mind without speaking.

In the physiological laboratories I was shown animals from which the caudate nucleus had been removed "completely" by Professor Clossofky. The animals exhibited no general motor abnormality several years after operation, but were slow at acquiring conditioned reflexes, i.e., they were slow to learn.

5. INSTITUTE OF NEUROSURGERY OF THE ACADEMY OF MEDICAL SCIENCES* DIRECTOR—PROFESSOR EGOROV

This institute, which was founded by Academician Burdenko before the war, has been enlarged recently and is now housed in an ancient palace. In 1943, at the time when the enemy was close to the gates of Moscow, I had first visited this institute. As I returned now, I recalled Nikolai Nilovich Burdenko, and his final toast to our Allied Surgical Mission:†

"I ask you to fill your glasses," he said, *"and listen to the few words I have to say: Our friendship must be closer. This is only the beginning of it. To our friendship in Science, in Life and in the World".*

There are 300 neurosurgical beds in the Institute now and patients are admitted only with a view to operation. Ten to twelve operations are carried out daily by a very large staff of neurosurgeons under the direction of Egorov. After the patients are admitted, however, they are studied by the neurologist and long-time friend of Burdenko, Professor Rappaport, and his six assistants; also by the neurophysiologist and electroencephalographer, Professor Rusinov.

Rusinov is in charge of neurophysiology here as well as being Deputy Director of the Institute of Highest Nervous Activity under Ivanov Smolensky. Rusinov stated that he has been much impressed with the clinical value of sound stimuli to increase electrographic evidence of abnormality in the human brain. He described the following interesting experiments on the effects of sound:

A direct electrical current was applied to the motor cortex of an animal so as to produce paralysis of the opposite foot. When stimulation was stopped, a succession of sounds in the animal's ear would produce a succession of movements in the previously paralyzed foot and this could be carried on for hours. He said that no epileptic after-discharge was produced. The sound "irradiates" in the brain so as to stimulate the cortical motor foot area.

He reported the case, also, of a woman who complained of phantom limb pain in an index finger. The finger had been previously amputated. When she was subjected to recurring sound stimuli the thumb next to the finger was made to move rhythmically.

6. DEPARTMENT OF THE PHYSIOLOGY OF HIGHER NERVOUS ACTIVITY OF THE STATE UNIVERSITY OF MOSCOW: L. G. VORONIN, PROFESSOR OF PHYSIOLOGY AND DEAN OF BIOLOGICAL SCIENCES

Like many other physiologists in Moscow, Voronin had come from Leningrad, where he was a pupil of Orbeli. In his new laboratories, adjacent to the recently completed University building, I saw impressive-looking Soviet electroencephalographs, and animal operating tables that would rival the best that any hospital could produce for the use of man.

Conditioned reflex studies are being conducted by S. Lagieve on fishes. About 32 trials will teach a fish to respond to two sound signals and one light signal. The response is to mouth one of two red balls and then receive food. When the problem is too difficult the fish develops a neurosis like other animals and swims away

*Address: 5 Tverskaia-Yaniskaia, 5, Moscow.

†Burdenko died in 1946 and his memory is held in reverence, for he was a real hero of Soviet Medicine—academician, neurosurgeon, founder of this institute, leader in medical research and education, winner of the Stalin prize—a blunt, warm-hearted man.

When I visited Moscow in 1943, it was as a member of the British-American-Canadian Surgical Mission. He was a Lieutenant General then, and Chief Surgeon to the Red Army. He was also Director of this Neurosurgical Institute, while Rappaport, Rusinov, Anokhin, and Egorov were on his staff there.

He had received us on numerous occasions, but the last occasion was a luncheon given for us in the institute, and Mrs. Burdenko was present. He wrote out the toast then that I have quoted.

from the stimuli or sulks at the bottom of the tank. "Every species," said Voronin, "has its own cleverness."

Dr. Krushinsky, in another of his laboratories, places a white rat in a glass box, shutting it in with a bell. When the bell is rung continuously the rat jumps with increasing excitement. Then he lies quiet in what is called a period of inhibition while the bell is silent. When the bell is rung again he has a generalized convulsive seizure. Following that the animal shows a sort of catalepsy, with a tendency to maintain postures for as long as 30 minutes. After, or during, this period, as I understood it, repetition of the sound may produce death due to small hæmorrhages in the midbrain.

Bromide will protect the animal, and thyroid extract as well.

Numerous other projects are under way to study the higher nervous activity of organisms, from fish to man, using conditioned reflex techniques, neurosurgical extirpation and other methods.

LENINGRAD

From Moscow to Leningrad we—the clever interpreter, Nicita Sannikov, who had gone with me on almost every expedition, Professor Smirnov and I—took the crack overnight train called the Red Arrow Express.

Leningrad is a beautiful city. It has some of the gay light of Paris, and the graceful waterways of Stockholm. But it has, too, a character all its own, for it is Russia of the far north and its byways, like its buildings, still echo the name of the heroic Peter.

It is a seaport city set on the banks and islands of the Neva River—the golden spire of the Admiralty at the end of Nevsky Prospect, the dome of St. Isaac's, the towers of St. Peter's and St. Paul's across the water, and the heroic equestrian statue of Peter the Great. The Winter Palace on one bank of the river and the Academy of Sciences on the other appear, no doubt, much as they did when Peter built them, for the surface scars of the siege of Leningrad are healed. The pictures by Russian painters of all periods have returned to the National Gallery and the Ballet's lovely fairy tales are danced again with all the reminiscent romance that this people love.

Pavlov's 106th birthday, the 27th of September, fell on the second day of our stay in Leningrad. He lies buried, with Mrs. Pavlov beside him, in Volkovo, the cemetery which is reserved for scientists and men of letters. His great predecessor in physiology, Sechenov, is buried there, also Mendeléev, Turgenev, and Dostoyevsky.

At 11 o'clock on a cold grey morning I stood in the rain beside the family enclosure while Pavlov's distinguished pupils, Orbeli, Bykov, Kupalov and others, laid wreaths in memory of the man. High above the grave was a bronze bust of Pavlov and below the bust his words of counsel to young scientists carved in the cold blue stone.

1. PAVLOV'S INSTITUTE OF PHYSIOLOGY OF THE ACADEMY OF SCIENCES*
DIRECTOR: ACADEMICIAN K. M. BYKOV

This institute is housed in a curiously curved building on the Neva River. From the front door a grand staircase of white marble leads upward to the second floor. As we climbed I could hear the faint echo of the barking dogs and I thought of how often Pavlov had himself climbed those stairs and savoured the familiar smells and sights and sounds. A superstitious dualist, if one had been present, might have fancied that the spirit of Pavlov was walking with us through this laboratory.

But indeed, in one sense, I met the spirit of Pavlov—the man that I had seen in the Nesterov painting, with fists clenched, longing to get on with the work—in every scientific institution that I entered. So many workers are trying to turn the key of the conditioned reflex in the lock, and thus to open the door to knowledge of the nervous system by means of this truly Russian method.

Professor Bykov has 25 different laboratories or departments under him including this building and the one in the country at Koltushi. At Koltushi experiments are carried out on various types of animals—chimpanzees and monkeys, bees and silkworms. An exhaustive study has been undertaken to decide whether or not conditioned reflexes are inherited by succeeding generations.

The principal preoccupation of Bykov is to study the functional relationship between the cerebral cortex and the visceral receptors which, he says, are important in all organs, including blood vessels and glands. Conditioned visceral reflexes, he pointed out, can be established by virtue of the fact that impulses reach the cortex from the viscera. Intero-receptors and extero-receptors control the dynamics of the cortex.

In one department Professor Soloviov was studying the digestive processes in dogs after successfully establishing two Pavlov pouches in each animal, one including the lesser curvature of the stomach and one of the greater curvature of the stomach. This is a difficult operation but the animals were in good condition and quite happy.

When bread was given to the animal the response was chiefly from the greater curvature pouch, milk arousing the other, and meat, both. When the pouches were denervated, the secre-

*Address: Nab. Makarova 2a, Leningrad.

tion diminished. Secretin has its effect through the nervous system. Bykov has a conception of neural and humoral overlap which I am quite unable to describe adequately.

When partial corticectomy is carried out, severe and long-continued decrease in secretion is produced by "premotor" removal of cortex and only a relatively brief decrease when occipital cortex is removed.

In another department, control of the peripheral vasculature was being examined. Electrodes were placed in the animal's skull and left in place so that the cortex could be stimulated at will. The limb was then enclosed in a plethysmograph so that changes in limb volume could be recorded. If the stimulating current was near the threshold required to cause limb movement, shrinking or enlargement of the limb might be produced.

Now if a bell was sounded each time the cortex was stimulated and food was given at the same time, the cortical stimulation could soon be dispensed with, and the sound of the bell would continue to produce the plethysmograph change as a conditioned reflex.

In similar ways they have shown that any part of the arc, which includes receptor, nerves and cortex, could be stimulated as a step in the establishment of the reflex. Many other examples could be given.

They pointed out that a conditioned reflex of an organ may constitute a pathological process. Thus, experimental organ-neuroses may be produced. Following this line of thought, certain clinical diseases may have a cortico-visceral reflex basis, e.g., hypertension, and gastric and duodenal ulcer. The glands and the blood vessels are included with other organs in such viscero-cortical interrelationships.

In studies of urinary secretion they have denervated an animal's kidneys to convert the urinary control into a humoral one, and in the reverse situation have studied nervous control of the kidneys in animals, after hypophysectomy which interferes with humoral control.

The chemical changes of the brain, which, it was said, could be detected as characteristic of the excitation or inhibition produced by conditioned reflexes, have been studied by quantitative chemical methods, and with the use of isotopes.

Bykov discussed the second signal theory as related to the thinking of men, pointing out that Pavlov had considered speech to be organized on the basis of conditioned reflexes under the influence of visual and kinæsthetic stimulation. Each conditioned stimulation was the signal of an unconditioned reflex and speech the signal of signals.

Professor Krassagorsky gave a boy of 10 years a piece of candy each time he heard the word four. When salivation was established as a reflex phenomenon related to the sound of four alone, the boy was presented with a problem such as to divide 8 by 2. Salivation would occur before the boy could pronounce the word four. Many applications of this form of study have been made to clinical patients.

Dr. Airapetiansk carried out the following experiments: Large amounts of water were run into the patient's rectum. This produced rapid diuresis. A bell was sounded while the rectal injection was being made. After a number of repetitions of the performance, the sound of the bell would produce normal diuresis, without rectal injection. Thus a cortico-renal conditioned reflex was set up.

The second experiment upon the kidney was carried out upon a dog. The ureter was catheterized and the renal pelvis dilated with water. Each time it was dilated, the dog was fed. Soon, dilatation alone would produce salivation without feeding. After that, the cortex in the vicinity of Brodmann's area 4, 6, and 8 was excised in one hemisphere. This caused the reflex to disappear as the result of dilatation of the contralateral kidney, but not for dilatation of the ipsilateral kidney.

Vestibular reflexes were also discontinued by contralateral corticectomy but not by ipsilateral.

Airapetiansk carried out other human experiments, as follows:

The urethra was catheterized and the bladder filled with fluid while the patient himself watched the indicator, of bladder pressure, that had been set before him. When the filling reached 100 c.c., the patient was aware that the bladder contracted and emptied itself. Soon it was found that, if the pressure gauge remained at 0, the bladder would not contract even when it was filled to 400 c.c. (i.e., four times the usual amount required to induce contraction); the patient felt no desire to void. On the other hand, if the gauge was caused to point to 100, he would void even though little or no fluid was injected into the bladder.

A patient who had a gastric ulcer, and suffered spontaneous contractions of the stomach, swallowed an intra-gastric balloon so that gastric pressures could be recorded and he could see the record. The man felt his stomach contract each time the gastric pressure gauge reached 5. Later on, if the patient could see that the gauge remained at zero, his stomach continued to be completely relaxed with no pathological contractions.

Colonel Galkin demonstrated two women who said they suffered from chronic pain. They had been relieved by intravenous injection of Nupercaine which was said to denervate the visceral receptors. The patients had gone to sleep and were relieved for considerable periods afterwards. Later injection, at least in the case of one of them, with intravenous saline was enough to relieve the pain and change the patient's whole behaviour for days in a remarkable manner. These studies are of interest,

regardless of the question as to whether the patients were hysterical.

Colonel Galkin also demonstrated surprising work that seemed to prove that an epileptogenic agent, such as camphor in oil, 20%, or Pyramidon in water, 4%, produced epileptic seizures in an animal by means of the effect of viscero-cortical afferent impulses acting upon the cortex and not because of the direct effect of the epileptogens upon the brain.

When the drug was introduced by intracarotid injection, no seizure resulted. When cats were now arranged for crossed circulation studies and the circulation of the brain of A was maintained exclusively by the heart-lung circulation of B, injection of the agent into the femoral vein of A produced seizures in A, although the blood of this animal passed to B and did not reach the brain of A. Injection of the agent into the pleural space of A also produced seizures in A. It was stated that the obviously necessary control experiments bore out the conclusion that the fits were produced by nervous impulses from heart and lungs to brain.

2. LESGAFT INSTITUTE*—DIRECTOR OF THE LABORATORY OF EVOLUTIONARY PHYSIOLOGY OF THE ACADEMY OF MEDICAL SCIENCES: ACADEMICIAN L. A. ORBELI

Since 1913 Professor Orbeli has been in charge of this laboratory, where he is surrounded by loyal associates, some of whom have worked there with him from the very beginning. The rooms are bright and spacious, the street is narrow and dingy. Since he relinquished the added direction of the Pavlov Institute to Bykov, he has had time and strength, at 73 years, to devote himself to research.

Among the problems studied here is that of the evolution of organs in young animals when nerve control of the organ had been interrupted. When the innervation had been interrupted and restored, the organ grew again in size and function. Comparative, ontogenetic, and embryological studies were in progress.

Pædiatricians on his staff were studying conditioned reflexes and unconditioned reflexes in children from the age of the premature infant to adult life.

Orbeli was interested in the inheritance of reflexes and in the fact that some unconditioned reflexes make their appearance after the time for the development of conditioned reflexes in children. He has made similar observations in patients while they were recovering from insulin coma.

Professor Moisievitch, distinguished-looking friend and long-time associate of Orbeli, is an enthusiastic histologist interested in ultraviolet light absorption. He took numerous photographs during the visit to the laboratory.

*Address: Prosp. Maelyna, 32, Leningrad.

3. NEUROSURGICAL INSTITUTE* DIRECTOR: SHAMOV. ASSOCIATE NEUROSURGEON: BOBCHIN

This is a neurosurgical hospital of 200 beds. It was obvious at once that there was great enthusiasm among the staff and that the clinical work is extremely active. The contributions to literature, since Molatkov founded this institute 30 years ago, are apparently extensive and numerous. Both Speransky (who is now at work in Moscow) and Beritov (who now works in his Institute at Trilsky, Georgia) carried out their early experimental work here.

Director Shamov is an experienced surgeon who studied neurosurgery with Harvey Cushing in 1913. The first institute building was destroyed by enemy bombs in the recent war, and they now occupy cramped quarters but have established a school for graduate students, through which nearly 2,000 men have passed. They control an extensive network of neurosurgery in other hospitals and have published "700 articles, 16 text-books and 8 monographs," statistics which were, I am sure, of interest to the news reporters who appeared in this institution at the time of my visit.

4. INSTITUTE OF EXPERIMENTAL MEDICINE OF THE ACADEMY OF MEDICAL SCIENCES† DIRECTOR OF THE PAVLOV LABORATORY: PROFESSOR P. S. KUPALOV

Active work on conditioned reflexes is in progress in this laboratory which was built by Pavlov and where he continued to work even after the Pavlov Institute was built, 15 minutes away, on the Makarov Embankment.

The Director, Kupalov, is a distinguished pupil of Pavlov. He speaks English and is the editor-in-chief of the Journal of Highest Nervous Activity. He is at present engaged in studying dogs after making an incision in the cerebral cortex all around the visual cortex. He found the general behaviour of the animals to be unaltered. They could be conditioned quickly to sound but conditioning to vision was slow, almost impossible. The dogs would seem to distinguish a cross from a circle but would not act on this discrimination and jump to the table. Anatomical studies of the brain are not yet completed for this work.

The visit to Leningrad closed pleasantly at dinner in the apartment of Professor Bykov who is a discriminating collector of paintings, especially of the Russian and Dutch Schools. When I inquired about food rationing in the days of the siege of Leningrad, Mrs. Bykov replied "400 grams of bread per day" and she picked up

*Address: Mayakovskaya Street, 12, Leningrad.
†Address: Kirovsky Prospect. 69/71, Leningrad.

four small slices of black bread. Professor Kupalov, who was a guest at the dinner, added quietly, "Half of the members of the staff of my institute died of starvation before the siege was lifted."

Many changes have taken place in the Soviet Union since 1943 when I made my war-time visit. Moscow has broader boulevards filled with roaring traffic. There are new towering apartments and a vast university. There are greater multitudes of people pouring into market and store, museum and mausoleum—people who are somewhat better dressed, whose pace is a little more leisurely.

The commodities that they buy resemble those of the West from refrigerator and television to teddy bear and cheap toy. The show-window parade of women's things—dresses and shoes and hats—are in styles as frivolous and modern, to my untutored eye, as those in any western capital. The church-museum is thronged with the curious, and the active church is crowded with fervent worshippers who chant and sing in moving harmony. Only the ballet has not changed and students stand all night in line for the tickets.

As I look back on that busy fortnight I realize that there is much less difference than there was between life in the U.S.S.R. and our life in the West. In medical science too there has been a parallel evolution.

We are closer to each other in methods and manner of thinking than we ever were. And yet a strange river of misunderstandings flows between us. So much good would come to them, as it would to us, if that river were gone, if there were no East or West.

Physicians, the world round, must hope that we have come to the dawn of a better day when fear will vanish like a mist and governments find a common goal. In Burdenko's words, "Our friendship must be closer . . . . friendship in science, in life and in the world."

Clinical and Laboratory Notes

PLASTIC HELMET FOR HEAD PROTECTION IN CHILDREN

T. A. McLENNAN, M.D., *Barriefield, Ont.*

THIS DESCRIPTION has been written in the hope that it may be of help to children with severe petit mal, cerebral palsy and other neurological conditions.

In 1950, when he was six months old, C.M. developed severe epilepsy of a mixed type. During the petit mal attacks, the patient's head would flex sharply forwards. These head jerks became so severe that constant attention was necessary to prevent trauma to the forehead from surrounding objects.

A hat designed for cerebral palsy was ordered from New York. It proved completely

Fig. 1

ineffective in protecting the forehead, although it was priced at $23. At this time the parents noticed a plastic racing helmet, of the type designed for children, in a war surplus store. It proved to be the answer to the problem. The helmet is made of strong but resilient plastic and it is able to absorb a tremendous impact before cracking. An adjustable plastic harness within enables it to be fitted to children from 2-12 years. It comes in six or more brightly coloured plastics and is socially acceptable to a small child. The price varies from $1.50 to $3.

During the summer, holes may be drilled through the helmet, in order to provide better ventilation. It may be painted a light colour to reflect the rays of the sun. During the winter the plastic becomes brittle and cracks easily when it is cold. This can be overcome by covering the helmet with elastic adhesive tape.

There is no doubt that the protection afforded has saved this particular child's life. As well, it has enabled him to develop normally, by participating in play with other children. This would not have been possible without adequate head protection.

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Editorials

HEALTH EDUCATION OF THE PUBLIC*

An interesting seminar on health education of the public was convened by the Commonwealth Government of Australia early this year. Some of the ideas which came out of this meeting may be of significance for Canada. In the first place, the meeting was that most useful type of seminar, a multi-disciplinary one, with medical practitioners, educators, nurses, dentists, nutritionists, sociologists, health inspectors, psychologists and publicity officers in attendance. Some guidance was also given by Miss Helen Martikainen of the Section of Health Education of the World Health Organization.

In the opening session it was suggested that in spite of the great advances in medicine and the relative security from epidemic disease enjoyed in well-developed countries, there were still many problems in health education to be solved. Perhaps the neuroses should be the next major problem to be attacked by public health people generally, though the complacency in civilized populations—due to their security from disaster—makes it more and more difficult to stimulate their interest in health and hygiene.

The health education of the public has always been recognized as one of the tools of public health practice; only the methods have changed, and therefore the main concern of this seminar was with methods and technique. There was much criticism of the effectiveness of existing methods of health education; the value of spending large sums of money on such things as pamphlets, books and posters was doubted in many quarters. A thought-provoking contribution to the seminar came from Dr. S. M. Brown of Sydney who discussed the social basis of learning, mentioning that in the primary schools of New South Wales graded courses in health education had been introduced into the general curriculum. Dr. Brown considered the basic principles of learning which were relative to health education in general. First came the need for the voluntary co-operation of the public; secondly, it must be remembered that the health educator was mainly concerned in changing attitudes and behaviour rather than in handing out information—informing people was not the same as educating them. Thirdly, the health educator's task was a struggle against apathy and indifference rather than against ignorance and hostility, though new ideas always present a personal threat to the learner. If health education was to be successful, said Dr. Brown, the approach had to be related to the goals and interests of the group aimed at. Building on such emotions as fear and anxiety would not yield good long-term results, nor should it be assumed that the public in general had a positive desire for healthful living.

The discussion groups drew attention to the fact that even civilized societies have subtle forms of folk resistance, with cultural characteristics sometimes opposed to the promotion of healthful living. Their attitudes and prejudices must be sympathetically studied and understood before an effective approach can be made. No one is better placed than the family doctor for acquiring an intimate knowledge of these attitudes and prejudices, and he is therefore an essential member of the health education team. The health educator must also realize that the level of understanding in some groups may be considerably lower than is at first apparent. The need for getting at official and unofficial community leaders as a spearhead for community campaigns was particularly stressed, though it must be remembered that these persons may be as steeped in prejudice as the rest of the community. An attack on small groups may well achieve a result when mass dissemination of information would produce no results at all. The difference between health education and commercial advertising in this respect is that the

* *M. J. Australia*, 1: 734, 1955.

commercial advertiser is trying all the time to gauge mass demand and satisfy it, not to change it radically.

The role of the different varieties of health education worker was thoroughly discussed at the seminar; here, as always, there was a certain difference of opinion. The main point of dissension was the question whether professional health educators were required or not, and what they should do. The general feeling was that the medical practitioner must control health education and that he should do this through such agencies as departments of health, the B.M.A., universities and the professions ancillary to medicine. The non-medically trained health education specialist should simply play the part of a co-ordinator, facilitating the work of other groups and helping in the organization of more extended activities. Some members of the seminar felt that there was no need to introduce this new specialty, but that health education should be built on the solid foundation of well-established professions. This is all very well, but it must be realized that if the physician neglects his responsibility for educating the public, someone else, less well-qualified save in technique, will step in and do the work for him.

Editorial Comments

HORMONES AND THE PREGNANT DIABETIC

The climate of opinion in some quarters is now unfavourable to the use of hormones during pregnancy in diabetics. It will be recalled that the suggestion was made many years ago that there was a state of disequilibrium as regards sex hormones in diabetic women, and that regular administration of stilbœstrol and progesterone to such patients was claimed to lower the fetal mortality rate from 40% to 8%. On the other hand, in a paper given at the B.M.A.-C.M.A.-O.M.A. annual meeting in Toronto last June, the English obstetrician, Peel, of London, mentioned that he had been concerned in a clinical trial of hormone therapy organized by the Medical Research Council of the United Kingdom and had found no significant changes as regards fetal survival from a control series.

The full story of this Medical Research Council clinical trial is now available (*Lancet*, 2: 833, 1955). The trial was designed to assess the effect, if any, of treatment by oral administration of stilbœstrol and ethisterone upon the fetal survival rate in pregnancy among diabetics. Patients were selected according to certain criteria; they had to be under 40 years of age and not more than 16 weeks pregnant at the beginning of the trial. Comparable groups of patients attending nine hospitals in the United Kingdom were stratified by age and parity and randomly divided into "hormone-treated" and "non-hormone-treated" groups. All the 76 hormone-treated and 71 controls were followed up for at least six months after delivery.

The frequency of stillbirth and neonatal death in the two groups proved to be almost the same (fetal death rate 24%-26%). There were four cases of congenital malformation in the treated group and seven among the controls. Diabetic control during pregnancy was equally good in the two series and the incidence of hydramnios, œdema and albuminuria was equal. There was no significant excess in toxæmia incidence in controls, and blood pressure ranges were comparable. Results of urinary assay suggest that the oral hormone preparations had been absorbed but that these had no effect on the pattern of hormone excretion associated with fetal loss.

It is concluded that oral stilbœstrol and ethisterone, in doses rising from 50-200 mg. per day for stilbœstrol and 25-250 mg. per day for ethisterone, do not reduce fetal mortality in diabetic patients and have little, if any, effect on maternal health in pregnancy.

CARDIAC CALCIFICATION AFTER HYDROCORTISONE

Two recent short communications from the University of California (*Nature*, 176: 503, 1955) mention an unexpected side-effect of hydrocortisone therapy in mice. The observations were made during experiments on transferable breast carcinomata. In these experiments it had been shown that hydrocortisone inhibits the growth of transferable tumours but shortens the survival time of the tumour-bearing animals. The unexpected finding was that mice surviving treatment with the adrenal hormone for 30 days developed deposits of calcified material in the myocardium. Further study was made of hydrocortisone injected into female mice, in a daily dose of 0.25-2.5 mg. On the day after the tenth injection the animals were killed and the calcium content and weight of the heart were determined. The hydrocortisone produced hypertrophy of the heart, as expected, but also raised the calcium content from 2.2 μg. per 100 mg. in controls to 6.4 μg. at the 0.25 mg. dosage level, 17.2 μg. at the 0.5 mg. level and 27.9 μg. at the 2.5 mg. level.

The deposits were granular and basophilic, chiefly confined to the ventricles where they lay within the muscle fibres. It remains to be seen

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whether there is any clinical inference to be drawn from these findings, which illustrate once more the fact that with hormones the effects obtained are widespread and not always desirable.

HÆMOPHILIA

In 1951 the Medical Research Council of the United Kingdom appointed a working party to advise them on problems associated with hæmophilia, and the working party recommended among other measures the preparation of a memorandum setting out the modern views on diagnosis and treatment of the various coagulation defects. Although hæmophilia is not a common condition, it does give rise to a great deal of anxiety on the part of the patient, his relatives and his physician, and the clear exposition by Drs. Macfarlane and Biggs in the memorandum* which has now appeared should prove extremely helpful to general practitioners somewhat bewildered by recent developments in this field. The authors give an elementary account of the probable defects of coagulation, with a special reference to hæmophilia, Christmas disease, defects of factor V and factor VII and afibrinogenæmia. They point out that the term hæmophilia should be restricted to the hæmorrhagic diathesis caused by deficiency in the blood of the specific clotting factor known as antihæmophilic globulin. As is well known, this deficiency is due to a hereditary (sex-linked recessive) defect. The incidence of affected males in the United Kingdom is given as 1-2 per 100,000. Christmas disease is probably only one-tenth as common as hæmophilia and is due to deficiency of a different factor also required for thromboplastin generation. It also is inherited as a sex-linked recessive character. Deficiencies of factors V and VII are usually not sex-linked and either sex may be affected.

In clinical diagnosis, the recognition of a hæmorrhagic state is the first step. A careful history both of the patient and of his family is essential. Any patient who has required transfusion after a tooth extraction is probably suffering from a hæmorrhagic diathesis, whereas any patient who has undergone a surgical operation, or a tonsillectomy or removal of several teeth without undue bleeding, is unlikely to have been suffering from a general hæmorrhagic disorder. In differentiating clotting defects from conditions in the purpura group, the authors mention that spontaneous bleeding such as oozing from mucous membranes or ecchymosis formation suggests purpura rather than coagulation defect. Abnormal hæmorrhage due to coagulation defect is not limited to skin and mucosa and is usually related to trauma or tissue damage. Signs and symptoms alone are of little help in distinguishing varieties of coagulation defect. If the hæmorrhagic state has existed from infancy, it is likely to be hereditary, even if there is no family history, for in about 25% of cases of hæmophilia no history of affected relatives can be obtained. A condition arising first in late childhood or adult life is unlikely to be hereditary. The authors discuss the laboratory diagnosis, which they consider to be relatively simple, and give full technical details.

They describe the treatment of coagulation defects as far from satisfactory. No general treatment other than transfusion of normal blood or of certain blood derivatives has given consistently encouraging results. In a deficiency state, the missing factor must either be replaced or its normal production by the body stimulated. The latter course is not yet possible. Continuous replacement therapy is not practicable and transfusion should be reserved for control of hæmorrhagic episodes or as a screen for minor surgical procedures. Although it has been stated that as little as 50 c.c. of plasma will restore the coagulation time in hæmophilia to normal for 24 hours, it must be realized that reduction of coagulation time to normal does not mean that the hæmostatic mechanism is normal. In order to render the thromboplastin generation test normal, a level of at least 30% of antihæmophilic globulin must be reached. This means that in most cases a volume of fresh normal blood at least equal to half the patient's blood volume must be transfused. Failures of transfusion are probably due to inadequate dosage. Intramuscular injection of antihæmophilic factor is useless; serum is also practically inactive.

As regards local treatment, the two important factors are pressure and a suitable coagulant; the two coagulants effective in hæmophilia are Russell's viper venom and thrombin. The coagulant should be applied on a dressing to the bleeding surface; pressure sufficient to stop the blood flow should be exerted for five minutes and the dressing then left in place. Stitching of wounds or of the gums after dental extraction is condemned. Conservative dental treatment must be given regularly to all hæmophilics to avoid the need for extraction, which must always be carried out in hospital with removal of not more than two teeth at any time. For deep hæmorrhage, transfusion is the mainstay of treatment. All surgery should be avoided unless essential for the patient's survival. Although intravenous injection seldom gives rise to trouble, intramuscular injection should be avoided.

This little monograph should prove very valuable to any practitioner who finds himself responsible for the care of one of these unfortunate and worrying patients.

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*Macfarlane, R. G. and Biggs, R. The Diagnosis and Treatment of Hæmophilia and its Related Conditions. M.R.C. Memorandum No. 32. Her Majesty's Stationery Office, London, $ .45.

ANÆSTHETIC SEQUELÆ IN THE ELDERLY

In a recent article, a British anæsthetist, Dr. P. D. Bedford,[1] presents unequivocal evidence that dementia in older patients may follow general anæsthesia. The anæsthetics given in the cases he cited were all general anæsthetics in which nitrous oxide was supplemented by other agents. Unfortunately some erroneous deductions concerning the deleterious effect of nitrous oxide have been made; it should in no way be inferred that the nitrous oxide was responsible for the dementia, but rather one or a combination of other factors present at the same time.

Before considering these other factors, nitrous oxide and oxygen anæsthesia may be briefly reviewed. Nitrous oxide is, as is well known, the mildest of anæsthetic gases in common use. When given with 20% oxygen, only anæsthesia of the lightest plane can be attained and this not until the nitrogen already present has been replaced. A higher percentage of oxygen will result in analgesia only. A more rapid induction or deeper plane production can only be brought about by invoking the deplorable and destructive aid of anoxia, unless supplementary drugs are used.

Following nitrous oxide and oxygen anæsthesia it has been the custom of many to administer 100% oxygen for a brief period. The wisdom of this has recently been shown by Dr. Fink.[2] He describes "diffusion anoxia" as that state of anoxia which occurs after anæsthesia when a patient is allowed to breathe room air. There occurs an outward diffusion of anæsthetic gases or vapours which lowers the alveolar partial pressure of oxygen. In the case of nitrous oxide the degree of anoxia so produced may last over 10 minutes, during which time the arterial oxygen saturation may fall below 90%. Such may be a precipitating factor.

These remarks concerning nitrous oxide are not aimed at criticizing it as an anæsthetic or analgesic agent; when handled with knowledge and understanding, it is of great value. It is indeed fortunate that the healthy individual is able to tolerate brief periods of hypoxia. One should, however, never take advantage of this fact or disasters will occur. Especially is this the case in older people when the cerebral blood flow may be decreased.

It appears that some are more predisposed to hypoxic insults than are others. All have seen or heard of the devastating effect of cerebral anoxia in younger patients; in older ones a shorter period of oxygen lack will produce similar effects and the result unfortunately is usually termed "senility".

Provided a brain has a blood flow able to carry to it sufficient oxygen and appropriate nutritional elements and to bear away the products of metabolism, it will continue to function so long as the vasculature is efficient—a man is as old as his arteries.

During anæsthesia, the "factors" referred to above which may interfere with the status quo of cerebral metabolism may be summarized as follows:

1. *Oxygen lack.*—(a) There may be obstruction of the air passages, at any level, from a variety of causes. (b) The oxygen lack may be the result of a low oxygen tension in the inhaled gases. (c) There may be inadequate ventilation due to different causes, such as coexisting pulmonary conditions, inefficient assistance to respiration after use of relaxing agents, potent anæsthetic agents or premedicant drugs which depress the respiratory centre. Postoperative respiratory depression may be caused by the excessive use of narcotics.

2. *Inefficient circulation.*—Hypotension may follow a number of incidents such as hæmorrhage, shock or deep anæsthesia. This may precipitate cerebral anoxia or a cerebral thrombosis. Hypotensive drugs and techniques, though of value in many cases, should receive very careful consideration before being employed in older patients.

3. *Posture.*—The possible adverse effect of operative posture on either ventilation or blood pressure should be remembered.

4. *Other factors.*—The clinical state as regards hydration, anæmia, nutrition, and vitamin status in older people should be studied. The presence of toxæmia or fever should also be noted because of the increased oxygen consumption.

The same principles should be considered from the point of view of the heart and coronary vessels. In addition to this, the detrimental effect upon the myocardium of an accumulation of carbon dioxide with concomitant rise in plasma potassium should not be forgotten.

From a clinical standpoint, the older patient should be made as fit as possible before operation. Before anæsthesia, premedication should be specifically prescribed to avoid respiratory depression. During anæsthesia adequate ventilation should be maintained at all times, while the blood pressure should be watched carefully and kept in the neighbourhood of its preoperative range. These principles should be kept in play during the postoperative period when a minimum of narcotics should be employed. A small amount of discomfort is a low price to pay for the maintenance of normal cerebration.

The actual choice of drugs and techniques used during anæsthesia should be based upon these principles.

REFERENCES

1. BEDFORD, P. D.: *Lancet*, **2**: 259, 1955.
2. FINK, B. R.: *Anesthesiology*, **16**: 511, 1955.

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WORLD MEDICAL ASSOCIATION

NINTH GENERAL ASSEMBLY

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THE NINTH GENERAL ASSEMBLY of the World Medical Association, held in Vienna, Austria, September 20-26, is now history. The setting for this Assembly was a happy one. Austria, who so recently regained her freedom as an independent nation of the world, is making a valiant attempt to take her place again as a leading nation in medical affairs. Vienna, long a Mecca for graduates and undergraduate students in the fields of medicine, music, and the arts, seems to be undergoing a rebirth both physically and spiritually. Everywhere one travelled in this magnificent city one saw signs of the repairing of the ravages of war and, more important still, the shedding of the yoke of occupation.

The Assembly meetings were held in the Neues Rathaus (New Town Hall), which is a magnificent example of Gothic architecture. The Rathaus had been made available to the World Medical Association through the courtesy of Herr Jonas, the Lord Mayor of the City of Vienna. Here in the large banquet hall, once the scene of world-renowned Viennese balls where the orchestra presided over by Johann Strauss and other noted musicians supplied music to the festive crowds, the President, Dr. Spinelli of Italy, convened the first session. It was also in this same great hall that the then Lord Mayor of Vienna received Hitler at the time of the Anschluss. This great hall hung with elaborate crystal chandeliers, the flags of the various member countries streaming from the balconies, the tables arranged facing the rostrum, each table containing the small national flags behind which were seated the delegates from the member nations, presented an inspiring picture. In the midst of this splendour one could close one's eyes and in imagination hear the strains of music of happier days as well as the sword clanking and heel clicking of the unhappy times through which Vienna has passed in our generation.

Arrangements had been made for simultaneous translation in the three official languages, English, French and Spanish, and facilities were also available for the use of the German language when necessary. The Canadian delegates were seated next to those of Denmark, with our Commonwealth brethren from Australia and South Africa immediately in front, and the delegation from Germany immediately behind us. As one glanced about the Assembly many familiar faces presented themselves: Sen of India, known to many in Canada through his participation in British Commonwealth Conferences, Macrae and Greig of Great Britain, Rasmussen of Denmark, Mallen of Australia, Lull and Murray of the United States of America, Knutson of Sweden, and many others. To those of us attending our first World Medical Association Assembly, to meet doctors from all over the world, representing all colours, creeds, and nationalities, was a stimulating experience.

ASSEMBLY SESSIONS

In his opening remarks Dr. Spinelli, the President for 1954-55, stated that in his opinion the one and one-half million physicians in the world could be, through well-organized activities, a tremendous force for peace and high moral levels throughout the world, and he called upon the physicians of the world to unite in the name of democracy. Dr. K. Niederberger, President of the Austrian Medical Association, welcomed the delegates in the name of the President of the Federal Republic of Austria, and in the name of his own Association. The Lord Mayor of Vienna, Herr Jonas, then declared the Ninth General Assembly officially opened. Dr. Hector Rodriguez, the secretary for Latin America and delegate from Chile, presented the standards and flags of the Chilean Medical Association.

Dr. Karl Niederberger of Austria was named President of the World Medical Association for 1955-56 and was installed in office by Dr. Spinelli. In his presidential remarks Dr. Niederberger stated that the Austrian Medical Association wished to contribute all it could to world medicine. He further stated that no matter what the World Medical Association does it should have only one aim, the alleviation of suffering humanity, and to be a true brother to our neighbours—"International co-operation is the commandment of our time."

Applications for membership in the World Medical Association were received from the Vatican Medical Association, the Venezuela Medical Association, and the Medical Confederation of Morocco. Their applications were recommended by the Council and confirmed by the General Assembly.

Dr. Dag Knutson of Sweden, chairman of the Council of the World Medical Association, reported on the activities of the Council during the year and projected new activities under consideration for the immediate future. Among others the following were the most important:

1. Programme to assist underprivileged countries and undeveloped medical associations.
2. Principles of co-operation between practising doctors and public health officers.
3. Development of a central repository for medical credentials.
4. Development of a medical emblem for doctors.

The regional secretaries' reports and those of the various committees were received and were approved by the Assembly.

Dr. Austin Smith, executive editor of the World Medical Association Journal, presented a report on the activities of the Journal (it was interesting to note that the Journal has its second largest circulation in Canada, this being surpassed only by the United States of America). The total number of copies circulated throughout the world was 14,000, and of these 1,667 were circulated in Canada. The Journal of the World Medical Association is not self-supporting and showed a deficit last year of $6,785.

Dr. Lionel Whitby, Chairman of the Committee on Medical Education, reported on the progress of his committee on arrangements for

the second world conference on medical education to be held in Chicago in September 1959. The theme of this conference is to be "The Training of the Doctor" and will therefore allow both undergraduate and postgraduate medical education to be considered.

Dr. Otto Leuch, treasurer of the World Medical Association, in presenting his financial report stated that in 1954 a small surplus of $935 was realized over income and expenditures. The United States Supporting Committee continues to pay the costs of the secretarial office in New York and the cost of publishing the Journal. These two enterprises last year amounted to $147,323.

In presenting the tentative budget for 1955 it was recommended that the 1956 subscription rate be set at 60 Swiss centimes per member, for 1957 80 Swiss centimes per member, and for 1958 one Swiss franc per member. These recommendations were adopted. It was interesting to note that there are at present 10 member associations who are paying at the rate of one Swiss franc per member and that Canada is one of these. In addition the Canadian Supporting Committee contribution for 1954-55 was $3,950. It would, therefore, seem that Canada is at present bearing her fair financial share.

The foregoing synopsis gives the highlights of the first two days of discussions. On the third day of the conference the morning was devoted to a Medical Editors' Conference and this was attended by the General Secretary of the Canadian Medical Association while your other delegate visited the Allgemeines Krankenhaus (the General Hospital of Vienna). This hospital was founded by Emperor Joseph II in 1782 by enlarging an almshouse. It is the birthplace of well-known methods of medical teaching. It was the hospital where the great Billroth did his work in the nineteenth century. I had the pleasure of meeting Professor Schonbauer, director of the University Surgical Clinic. He kindly turned me over to one of the senior surgical assistants, who spoke English, and I was shown part of the hospital. The hospital occupies one whole city block and is a very old building, badly overcrowded, and by our standards lacking in modern equipment. I witnessed, in one of the operating rooms, a gastrectomy for gastric ulcer. Although Billroth's statue looks down on all who enter the gates of the hospital, the operation done was a posterior Polya type of resection and I was told that the Billroth I operation, in spite of its revival in many parts of America, is no longer done here. The operating room and its equipment by our standards were antiquated, but I was favourably impressed by the surgery carried out. There was a conspicuous absence of blood hanging in bottles from standards and, by the same token, a noticeable lack of blood on the floor and on sponges. The man was a good surgeon!

At the next general assembly session, Dr. Dag Knutson, Chairman of the Social Security Committee, presented a classical paper entitled "Social Security in the Field of Health Care—Its Background and Prospects." This paper, couched in beautiful English, should receive wide publication and would be a nice contribution for the *Canadian Medical Association Journal*. Following the presentation of this paper

Canadian delegates, Dr. E. K. Lyon and Dr. A. D. Kelly, at a session of the Ninth General Assembly, W.M.A.

the whole day was spent discussing social security in the various countries. Twenty-six different speakers participated in this discussion. These discussions ranged all the way from the very unsatisfactory situation as its exists in Austria, where less than three months ago the organized medical profession staged a "strike" for two days in order to bring their plight forcibly to the attention of the Austrian people and Austrian government, to the optimistic and glowing report from Australia of what was described as the "Golden Age of Medicine in Australia". One point in the discussion on social security which seemed pertinent to all countries was the increase in the cost of medicaments and the tendency of the medical profession to over-prescribe.

As this lengthy discussion went on, one could not help but be impressed with two things:

1. There seemed a great fear of their governments by those taking part in the discussions. Apparently co-operation between the profession and the government social-security planners in many countries is non-existent, and the profession is constantly fighting laws and regulations produced without any consultation with the existing medical associations. This is in contrast to our own country where to date the medical profession has been consulted on major changes in our social-security laws, particularly those which apply to health, and where our present Federal Minister of Health and Welfare has repeatedly stated that no major changes would be made without first consulting the medical profession. Such a partnership between medicine and government seems non-existent elsewhere.

2. In those countries where the medical profession finds itself entangled in social-security laws unfavourable to the profession, it was my impression that there had, in most instances, been a woeful lack of medical organization and a negative attitude towards assisting in the planning of changes in social security as applied

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to medicine. We, in Canada, have taken a positive view of the problems in our country and have at every instance to date been willing to co-operate with our governmental leaders in producing changes in our laws to meet the changing times. After this long discussion, which at times became very tiring, I found at the end of the day written across my notebook in my own handwriting and underlined *"Thank God I practise in Canada!"*

The final session was conducted on Sunday morning and the Canadian delegates for the first time found their voices and took part in the final discussions. Dr. Fernandez Conde of Cuba was named President-elect. Tenth General Assembly is to meet in Havana, Cuba, on October 9, 1956, and the Eleventh Assembly is planned for Istanbul in September 1957.

SOCIAL FUNCTIONS

The social functions of the Assembly are worth mentioning, for it is a well-recognized fact that one of the great benefits of any meeting of medical men is the contacts made not only across a conference table but at the receptions and dinners held in conjunction with these meetings.

The World Medical Association committee in charge of social events had arranged a full programme of sight-seeing, fashion shows, and visits to museums and art galleries for the ladies who accompanied their husbands to Vienna.

A reception for the delegates was tendered by the Lord Mayor of Vienna in the Rathaus after the first day's session. Following this the delegates and their wives were taken by bus to Grinzing, a suburb of Vienna, which is the seat of the wine industry of Austria. Here we were served a fine supper of cold cuts and sampled the new wine.

The following evening we were entertained by the Chas. Pfizer Company at a reception in the Palais Pallavicini, one of the old Viennese palaces now used as a club, and apparently one of the centres of the social life of Vienna. After the reception a special performance by the Vienna Philharmonic Orchestra was staged in the Grosser Musikvereinssaal, and the orchestra, under the baton of Professor R. Moralt, played to a packed house. The music hall is very ornate and like all public buildings encountered in Austria has a seemingly endless staircase to be climbed before reaching the auditorium. The orchestra was excellent and their rendition of the Blue Danube especially fine.

Late the following afternoon the delegates were taken on a visit to the Vienna Boys Choir School. This is an interesting institution and corresponds in many ways to our boarding schools. The boys enter the school at six years of age and are chosen from all strata of society. They are not only trained in music at the school but also receive a grade-school education. When they reach adolescence and their voices change, the ones showing promise are given further musical opportunities and high-school education, and following graduation an attempt is made to find them suitable occupations. The weather was perfect, and the choir entertained us beneath the trees in the garden. It was an inspiring sight to see these young boys perfectly disciplined and with beautifully trained voices respond in song to the baton of their teacher. Their rendering of Brahms' Lullaby and other selections left even the most uninformed musicians among us with a feeling of hope for the world. Only one thing seemed unnatural—not once during their appearance did I see one of these boys smile. I wonder why?

Following this we were again ushered to a reception, tendered by Mr. K. Maisel, the Federal Minister for Social Administration, at the Government Buildings. The following evening at the Théâtre de Wien we heard the Mozart opera "The Abduction from the Seraglio," which was extremely well done.

The final afternoon in Vienna, the delegates and their wives were conducted by bus through the Vienna woods of world-wide fame. At this stage of the year they were very beautiful—large expanses of green-wooded slopes with here and there a tree in autumn colours. En route we visited a very old monastery run by the Cistercian order and saw their very old church, chiefly noted for its beautiful stained-glass windows. We also visited Mayerling, made famous by the death of Prince Rudolf and his friend in the latter part of the last century. The famous hunting lodge where the tragedy occurred is now a chapel and cloister operated by the Carmelite Sisters. On the return trip we passed through Baden which was the headquarters of the Russians during the Occupation. The Russians had left the area just two weeks before our visit and the town appeared to have not yet begun to recover. The houses and estates seemed in a bad state of repair and we were told that before leaving the Russians removed almost everything, including the bath fixtures. Between Baden and Vienna lies the chief grape-growing portion of Austria, with vineyards as far as the eye can see.

The Ninth General Assembly came to a close on Monday evening, with a final dinner for the delegates and wives at the Auersperg Palace. This is a very elaborate old palace occupied in happier days by the Auersperg family. Like many other old-world palaces it is now used for reception and social functions and again, wandering through its beautiful rooms and courtyards, one could imagine oneself in the past and see again the elaborate balls and musicales held here when Vienna was the musical and cultural centre of Europe. Owing to the fact that the delegates were seated in a number of small rooms, it was impossible to hear the after-dinner addresses but sometimes this is a blessing.

GENERAL OBSERVATIONS

The meeting together of medical men from over 50 nations with an interchange of ideas, social contacts, and the understanding of the problems of our brother practitioners with no regard to race or creed, must be a powerful force for good in the world. It was my opinion that in spite of different approaches to the problem the doctors of the world have still one common objective, the alleviation of mankind's suffering. In order to do this well it is the opinion of the doctors of the world that the dignity of our profession as a whole and that of the individual doctor must be upheld and not subordinated to bureaucracy.

It was also my impression that when the medical profession finds itself in an untenable position with its government, the profession itself must shoulder part of the blame. A poorly organized profession with a negative attitude toward changing social conditions can expect interference by government. This is perhaps the greatest lesson to be learned from our confrères at this Ninth General Assembly.

Is the World Medical Association fulfilling the purpose for which it was established? I believe I can answer that with a qualified "yes." I believe there is still a great deal to be done. In the nine years since its formation the World Medical

Association has necessarily moved slowly and cautiously. I believe the foundations have been solidly laid and the organization is now ready to tackle problems which are still unsolved: (1) The assistance of the education of doctors in the so-called underdeveloped countries—a term used, and badly, to refer to many parts of Asia, Africa, and Latin America, where medical care is still far from adequate for the immense population of these countries. (2) The more equitable distribution of doctors: Austria has one doctor for every 320 people in Vienna, and yet India and parts of Africa are without adequate medical care. (3) The assistance of exchange students in medicine. (4) The assistance of national medical societies who because of financial or other difficulties find it difficult to take their rightful place in the councils of the World Medical Association. (5) The further elucidation of ethical problems in medicine in both peace and war. (6) Last but not least, the use of every means at the disposal of the over 600,000 doctors now affiliated with the World Medical Association to assist in maintaining the peace of the world.

Unless these and other humanitarian problems engage the immediate attention of the World Medical Association, I would fear that this great organization may develop into a debating society and miss a great opportunity for fulfilling its true objective.

I believe the Canadian Medical Association should continue its support of the World Medical Association. The individual doctors in Canada can best assist in this cause by supporting morally and financially the Canadian Supporting Committee. It was with some measure of pride that your Canadian delegates noted that nearly $4,000 was raised this year by the Canadian Supporting Committee. I believe those in charge of this fund have been wise in waiting for some special project before turning it over to the World Medical Association.

FOURTH GENEVA CONVENTION

Dr. J. P. Schoenholzer, official representative of the Red Cross at the 9th General Assembly of The World Medical Association in Vienna, discussed the 4th Geneva Convention of 1949. He pointed out that the convention was drafted and adopted in 1947 and modified and ratified unanimously by the representatives of 71 countries in 1949. However, to make this convention binding upon the nations, the signatures of the delegates must be ratified by the government of each country.

To date, 40 states have ratified the 4th Convention; 9 states have signed it; 8 states have indicated adherence to the convention through formal channels and only 21 of the original signatures have not yet been ratified. The countries that still have not ratified the 4th Geneva Convention are: Afghanistan, Albania, Argentina, Australia, Bolivia, Brazil, Canada, Ceylon, China, Colombia, Ethiopia, Greece, Iran, Ireland, New Zealand, Paraguay, Peru, Portugal, United Kingdom, Uruguay, Venezuela.

EDUCATION EXCHANGE FOR DOCTORS

The 9th General Assembly of The World Medical Association recognizes the advantages of an expanding exchange of well-qualified doctors between countries as a means of improving medical education and medical care.

Such an exchange not only benefits the profession on a national level but also serves to promote better understanding among the doctors of the world.

In the hope of promoting this objective, The World Medical Association endorses the resolution adopted by the 5th National Assembly of the Medical Federation of Ecuador.

The W.M.A. will therefore try to secure the co-operation of all its member associations in establishing an educational exchange programme for doctors wishing to widen their experience through study in foreign countries with the ultimate aim of promoting better medical care and medical education within their own country.

The Secretariat, with the assistance of the national medical association in each country, will compile lists of educational opportunities available in each country and circulate this material to other member associations.

TWELVE PRINCIPLES FOR SOCIAL SECURITY SCHEMES

The 9th General Assembly of The World Medical Association noted that it is becoming increasingly apparent that the organizers of social security schemes frequently do not recognize or adhere to the criteria established by The World Medical Association in its *Twelve Principles on Social Security and Medical Care*. The World Medical Association *again* invites attention to these twelve principles which are reproduced below.

TWELVE PRINCIPLES OF SOCIAL SECURITY AND MEDICAL CARE

Adopted by the Second General Assembly of The World Medical Association, 1948, reaffirmed by the Fourth General Assembly, 1950, the 6th General Assembly in 1952, and the 9th General Assembly in 1955.

Whenever medical care is provided as part of social security, the following principles should govern its provisions:

1. Freedom of choice of physician by the patient. Liberty of physician to choose patient except in cases of urgency or humanitarianism.

2. No intervention of third party between physician and patient.

3. Where medical service is to be submitted to control, this control should be exercised by physicians.

4. Freedom of choice of hospital by patient.

5. Freedom of the physician to choose the location and type of his practice.

6. No restriction of medication or mode of treatment by physician except in case of abuse.

7. Appropriate representation of medical profession in every official body dealing with medical care.

8. It is not in the public interest that physicians should be full-time salaried servants of the government or social security bodies.

9. Remuneration of medical services ought not to depend directly on the financial condition of the insurance organization.

10. Any social security or insurance plan must be open to the participation of any licensed physician, and no physician should be compelled to participate if he does not wish to do so.

11. Compulsory health insurance plans should cover only those persons who are unable to make their own arrangements for medical care.

12. There shall be no exploitation of the physician, the physician's services or the public by any person or organization.

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PUBLIC RELATIONS FORUM

Conducted by L. W. HOLMES,
Assistant Secretary, C.M.A.

VI. ENTER THE PATIENT

THE STAGE IS SET. The reception room, bright and cheerful, is empty except for the receptionist behind her desk. The doctor is in his office. Then, enter the patient. Suddenly all the forces of good or bad public relations are loosed. This is the moment when, in the interaction of personalities, the doctor's goodwill wanes or waxes. This is the moment of person-to-person contact, the basis of all human relations problems from onset to conclusion.

Who are the principals in this social interplay?

The *patient*—perhaps a businessman, a clerk, a housewife. Each, in his own sphere, is an adequate, perhaps expert, individual. But this identity is lost the moment he passes through the doctor's door. He has entered a strange and mysterious world of sickness, suffering, pain and death. It represents something fearful and unwanted. He harbours many feelings: fear, anxiety, embarrassment, hope, despair.

The *doctor*—he may come in many types: the bombastic, the majestic omnipotent, the calm confidential, the jocular, the bluff, the shy, the aggressive, the belligerent. He may be struggling for success; he may be at the peak of achievement in his field; he may be caught in the crush of time versus service; he may, himself, be tired, unwell, unhappy, worried, anxious.

These are two individuals of unlike personality and purpose at that time. In normal social intercourse each would make sacrifices in the interest of harmony. But the doctor-patient relationship is not a normal one. And, if harmony is to be achieved, the doctor must submerge his personality, adjusting to that of the patient. How the doctor acquires this facility is a problem only he can solve. There are no hard-and-fast rules, no yardsticks in the game. There are, however, many ways in which he may impress upon the patient his desire to serve only the patient's interests.

Let's start with the receptionist.

She should be trained in the art of welcoming people. Patients have a right to expect courtesy in the doctor's office. They have come, as consumers, to purchase medical service. When the doctor is ready to see the patient, the receptionist should usher him into the office. If he is a new patient introductions should be made, just as if a guest were being introduced to a host. The doctor should be certain to get the name right.

Another method is to have the receptionist precede the patient by a few seconds, taking the patient's card to the doctor. The doctor is then in a position to welcome the patient by name without waiting for an introduction.

If he has no receptionist, the doctor himself must assume the full responsibility for greeting the patient. After checking his appointment book to discover which patient is next, he can step to the door of his reception room and with a friendly smile announce the patient's name in such a way as to indicate a greeting and that the doctor is ready to see him.

A valuable adjunct to this programme for improved human relations is personal knowledge of the patient, his hobbies, his interests, his family. Keywords on the patient's card will give the doctor a clue to these aspects of the patient's life and permit him to launch his interview with the niceties of friendly patter.

What is the patient's first impression as he enters the doctor's inner sanctum? Is the doctor sitting back with his feet up on a partly-opened drawer? Is there a cigarette burning in an ashtray piled high with butts? Is the doctor sitting in his shirt sleeves? Is equipment scattered willy-nilly around the office?

These are actual patient observations which create unfavourable impressions. Certainly, the doctor who is interested in impressing his patient with his professional manner will guard against the many unprofessional practices which may be summed up in the following words of criticism: "sloppy", "dirty", "inconsiderate", "discourteous".

Now to the interview. The good-will and friendship of the patient will not be won in a hurried, five-minute interview, or with the quick scribbling of a prescription. Here are some suggestions from a number of doctors on how to give the personalized treatment which a patient has a right to expect:

1. Cultivate calm, assured manner.
2. Show interest in the patient.
3. Give evidence of sympathy, yet retain control of interview.
4. Give full attention to the patient. People soon lose confidence in the "absent-minded professor" type of physician.
5. Take time to listen patiently.
6. Use simple language.
7. Give each patient adequate time.
8. Be frank and honest; if you don't know, admit it.
9. Give satisfaction.

When the patient enters the doctor's office he has four questions in mind—frequently unasked. "What's wrong with me?" "What can you do for me?" "How long will it take?" "How much will it cost?" The doctor should anticipate these questions and answer them as honestly as he can—either directly or by implication. Of course, should he feel that the patient would not benefit from a full answer to some of the questions, he may have to hedge. But he must at least satisfy the patient—not just for the present but for the future.

It is dangerous for a doctor to assume that his patients are unable to understand things medical

and therefore to shove diagnostic and therapeutic ideas down the unquestioning patient's throat. In this day of a glut of medical articles in daily, weekly and monthly lay publications, it is only natural that non-medical persons have acquired some medical knowledge. Whether one believes this good or bad, it is safe to say that an intelligent patient, given an honest factual account of his illness together with a few of the necessary basic facts about anatomy and physiology, is a better patient. True, frequently patients are the victims of partial knowledge, sometimes incorrect knowledge. It is the physician's place to correct these notions. Health education is, after all, one of the responsibilities of the medical profession.

Every physician should have a simple medical vocabulary with which to explain to the patient his condition and what the treatment may be expected to do. He should not guarantee treatment results; malpractice actions can result if failure occurs.

When the interview with the doctor is concluded and the patient has been given an opportunity to ask any questions he may have, it is time for the friendly farewell.

If the patient requires another appointment, the doctor or his assistant should schedule it and write out a reminder card for the patient.

One doctor insists that no patient leave his office without physical evidence of the visit. It is usually a single sheet of paper—not a prescription—a typewritten or legibly penned list of instructions. This obviates the patient's forgetting or misunderstanding verbal instructions.

The same friendliness that characterizes the welcome should be shown by the doctor and his staff when the patient leaves the office. It is nice if the doctor can take the time to walk to the door with his patient. The patient should leave with the feeling that he has received not only the best medical care, but has been treated as an important individual.

Most important, the patient should leave the doctor's office with the realization that the doctor is a human being practising an honoured profession, not a magician who deals in the mystical.

The final question in the patient's mind—"How much will it cost?"—has not been discussed here. This very important question will be treated in a future article. Similarly, the problem cases which come into the doctor's office, the talker, the demander of new treatment, the belligerent, the shopper, will be taken up in other articles.

FORTHCOMING C.M.A. MEETINGS

1956 Quebec—June 11-15 (Ecole de Commerce.)
1957 Regina—June 17-21.
1958 Halifax—June 15-19.
1959 Edinburgh—July 16-24.
(Conjoint Meeting with B.M.A.)
1960 Banff—June 13-17.

GENERAL PRACTICE

A SURVEY OF GENERAL PRACTICE IN CANADA

To be undertaken jointly by
The College of General Practice of Canada and
The Department of Preventive Medicine of the Faculty of Medicine of the University of Toronto

REASONS FOR THE SURVEY

THE FAMILY is the basic unit of our culture and society. A good family doctor is basic to good medical care. He is able competently to deal with 80 to 90% of the ills of people and know when and where to get help for the remainder. One of the most essential things in medical care today is a good family doctor service. The services of an able family physician should be available to all the Canadian people if they are to get the type of service they should have at a price they can reasonably afford to pay. But the general practitioner of medicine today is having more difficulty than he should be having in providing the medical care he would like to give to his patients. Along with amazing progress in medical science has come a remarkable expansion of hospital facilities and just as marked a growth of specialist services. Though there is not the slightest quarrel with these developments, they do point up the fact that there has been a lack of comparable emphasis on general practice.

This is not a realistic approach to the broad field of medical services in Canada, because probably nearly half of its citizens live where the general physician has the whole field to himself. Moreover, the family doctor, whether in city or country, gives services that have unique and special values. For instance, he should be the most important member of the medical team in terms of continuing medical care, in assessing the health needs of the family as a unit and in the treatment of chronic diseases.

We are convinced that the special needs and possibilities for competence in general practice have not been fully appreciated either by the public or by the profession. We believe that general practitioner service has much more to offer than is being offered today. But suggestions for helping the family physician must be based upon the fullest possible knowledge. We feel that a survey of general practice is necessary if we are to wisely indicate how his present services may be improved and to plan new services for him.

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OBJECTIVES OF THE SURVEY

The survey will be a critical, analytical study:

1. To determine the kind of general practice needed by the Canadian people.
2. To elicit the type and volume of illness treated by general practitioners.
3. To determine how such illnesses are treated.
4. To study methods of office organization and management in general practice.
5. To determine how well present-day medical education prepares doctors for general practice. This would include an assessment of training of undergraduates and interns for general practice, and of postgraduate courses and facilities for the continuing instruction of general physicians. It would recommend possible improvements in training for general practice and perhaps even indicate the type of man most likely to succeed as a family doctor.
6. To learn the effect of various social and community influences.
7. To determine whether general physicians working together are able to give better medical care than if working separately. What kind of group practice is best?
8. To relate and determine the effects of voluntary and government medical and hospital care plans on general practice.
9. To learn how the general physician can best be integrated into his neighbourhood general hospital, whether large or small. What role should he play in hospital practice?

METHOD OF STUDY

The survey would be undertaken by a well-qualified general practitioner or internist, who would visit each doctor for a few days. He would be with the practising physician while the latter interviewed his patients in his office and visited them in their homes and in the hospital.

In the detailed study of each doctor's practice an evaluation would be made of:

1. His educational background, including his undergraduate and postgraduate training.
2. The quality of the history taken and the records kept.
3. The quality of the physical examination.
4. The laboratory work undertaken.
5. The treatment advised with the responsibilities accepted and procedures undertaken.
6. The conditions under which he works, including equipment and ancillary help.
7. The educational programmes for practising physicians encountered.
8. The differences in single, partnership and group practices.
9. The influence of prepaid medical and hospital care plans.
10. The extent of the practice of preventive medicine.
11. His relationships with hospitals, specialists, public health officials and colleagues.

THE PLAN OF STUDY

If general practice is to be understood and valued there must be a close personal study of individual practices under significantly different conditions. This would include a study of general practices chosen by random sampling of doctors in different age groups and in various localities such as large urban, smaller urban, well-populated rural and outpost rural areas.

Before the study the director will be asked to visit Dr. Osler L. Peterson who is conducting a survey of general practice in North Carolina under the auspices of the University of that state, and also interview Professor Oswald Hall, head of the Department of Sociology at McGill University, and learn of his findings in a survey of different types of patients in Montreal.

It is recommended that the study be undertaken in three phases or stages:

PHASE 1

This would be devoted to the organization of an office, to securing personnel and the preparation of forms and survey materials, and their trial on a group of ten to twenty general practices of varying degrees of competence in the Province of Ontario. This will be in the nature of a "pilot study", to determine the best mechanisms for securing the desired information followed by an evaluation of the usefulness and reliability of the data obtained.

In a review of the data from this study the records of prepaid medical plans, such as Physicians' Services Incorporated (P.S.I.), and of medical welfare plans for the indigent would be sought, so that these could be correlated with the individual practices being studied. This would help to indicate how typical or atypical these practices appeared to be in relation to all general practitioners on the rolls of P.S.I. and the welfare plans.

It is hoped that by using the experience of the North Carolina study this phase of organizing the survey and conducting the "pilot study" could be completed in about six months.

PHASE 2

This would include a study of general practices in a number of provinces or geographical areas of Canada. For example, the Province of Quebec, the three prairie provinces and the four Atlantic provinces might each be considered as units. This would be aided by the co-operation and support of the Provincial Chapters of the College of General Practice. The sample of general practices for study will be chosen by competent medical statisticians and will take into account such factors as age, sex, and distance from teaching centres. It is expected that the number of practices that can be conveniently and thoroughly studied will number approximately one hundred.

At the end of this phase a complete analysis of the findings will be carried out before proceeding to the next stage.

PHASE 3

This will be an extension of the study of important features that seem to require further clarification. It might be necessary to confine the scope of this investigation to a few important items. This phase would also include preparation of the report of the study for publication.

ORGANIZATION OF THE SURVEY

The Survey is a joint undertaking by the College of General Practice of Canada and the Department of Preventive Medicine of the Faculty of Medicine of the University of Toronto. It has the support and active participation of the Canadian Medical Association.

The Canadian Life Insurance Officers Association has donated $10,000 to the College of General Practice for this purpose. Reasonable assurance has been given that a similar sum will be granted next year if satisfactory progress is being made.

Steering Committee: Drs. C. Rose, Aurora, Ont., General Practitioner; P. A. Kinsey, Toronto, General Practitioner; T. Tweedie, Hamilton, Ont., General Practitioner; W. C. Cowan, Richmond Hill, Ont., General Practitioner; A. F. W. Peart, Assistant Secretary, Canadian Medical Association, Toronto; C. W. Farquharson, Toronto; Milton Brown, Professor of Hygiene and Preventive Medicine, University of Toronto; J. A. MacFarlane, Dean of Faculty of Medicine, University of Toronto; Wendell MacLeod, Dean of College of Medicine, University of Saskatchewan, Saskatoon; Chester Stewart, Dean of Faculty of Medicine, Dalhousie University, Halifax; Jean-Baptiste Jobin, Dean of Faculty of Medicine, Laval University, Quebec; W. V. Johnston, Executive Director, College of General Practice, Toronto.

Consultants: Drs. F. W. Jackson, Department of National Health and Welfare, Ottawa; C. D. Gossage, Confederation Life Association, Toronto; Harding leRiche, Medical Research Officer, Toronto.

It is anticipated and estimated that an annual budget of $50,000 for three years is required for a really comprehensive study of general practice in Canada. Such an expenditure is necessary because the study will require a full-time director, one or more associates and considerable statistical and clerical assistance.

We believe these funds can be obtained, and we wish to appoint a full-time director as soon as such a person is available. Following advertisements in several medical journals there have been a number of applicants for this position. Those interested in this appointment may be assured that it is not a blind-alley position but rather one that could lead to various attractive fields.

THE HALLMARK OF A HOSPITAL SERVICE

AT THE ANNUAL CONVENTION of the Ontario Hospital Association on October 25, 1955, Dr. Kenneth B. Babcock, Director, Joint Commission on Accreditation of Hospitals, Chicago, addressed an audience that filled the Ballroom of the Royal York Hotel.

The Joint Commission on Accreditation of Hospitals was created by five medical and hospital organizations—the American Medical Association, the Canadian Medical Association, the American College of Surgeons, the American College of Physicians, and the American Hospital Association. It is an independent voluntary non-profit organization, organized to render a public service. Its main purpose is to improve the quality of care rendered to patients in hospitals. It does so by establishing minimum standards of quality of patient care and then invites all hospitals and physicians to meet or surpass those standards.

The present programme is 2½ years old. Before that the American College of Surgeons spent $2,000,000 on a similar programme but it became too costly for them. The present programme is an improvement over the old one in that its standards deal with patient care of all sick people and not just surgical cases. Moreover, it places great stress on the human factors rather than on brick and mortar. The programme is a study of medical care in hospitals. Any hospital is eligible to come within its programme if it has been functioning and organized for a year and has a capacity of 25 or more beds.

The surveyors report directly to the Director and he in turn sends a report to the Commissioners of the Joint Commission on Accreditation of Hospitals. If they give unanimous approval, the hospital is granted accreditation. This procedure usually takes from 60 to 90 days.

The surveyors are not policemen. Their task is to report objectively on the facilities and the personnel of a hospital. About three-quarters of the stress is placed on the personnel. Their standards are minimal.

A number of hospital services are always investigated:

1. The maternal death rate is determined. It is expected to be no more than ¼ of 1% but it might be 2% with no criticism justified. To judge this, the cause of the maternal deaths must be clearly indicated.

2. Sterilizations. There is considerable variation in the practice permitted in this field, but the Joint Commission insists that there must be consultation in each case and that the hospital have its own rules clearly stated.

3. Anæsthetic deaths.

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4. Tissue committee. There is no such thing as acceptable normalcy unless it is shown clearly that it was justifiable. In other words, a report of the diagnoses must be available along with the report of the tissue committee.

Dr. Babcock stated that there are four R's to accreditation: A hospital must live up to its responsibilities; it must have rules; it must have records; it must have reviews.

General Standards

General standards for accreditation:

1. A good physical plant and efficient administration.

2. Restriction of the hospital medical staff to physicians and surgeons who are competent and ethical.

3. The maintenance of complete medical records of each patient.

4. The medical staff is permitted to practise according to written rules and regulations which are subject to the ultimate authority of the hospital governing board.

5. Medical supervision of the staff to assure that each member is restricted to what he is competent to do. V.W.J.

MEDICAL SOCIETIES

ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF CANADA

The annual meeting of the Royal College of Physicians and Surgeons of Canada was held at the Château Frontenac, Quebec, on October 21 and 22. On October 21 there were morning and afternoon sessions of the Divisions of Medicine and Surgery, with an annual meeting later in the afternoon. On the Friday morning an address on "The Effect of Hydrocortisone on the Healing of Wounds of the Brain" was given by Dr. Armando Ortiz-Galvan of Montreal, who is the 1955 medallist of the Royal College of Physicians. On Friday afternoon Dr. Ian B. Macdonald of Toronto gave a lecture on "Experimental Studies with Homologous Renal Transplants". Dr. Macdonald is the 1955 medallist of the Royal College of Surgeons of Canada. On Saturday there were morning sessions of the Divisions of Medicine and Surgery and also a session of the Section of Obstetrics and Gynæcology. On Saturday afternoon there was a scientific meeting chaired by Dr. John Hepburn, this year's President of the Royal College. The lecture in medicine at this meeting was given by Dr. Ronald V. Christie, Professor of Medicine, McGill University, who spoke on "Dyspnœa". He was followed by Dr. Harold B. Atlee, Professor of Obstetrics and Gynæcology, Dalhousie University, who lectured on "Surgery of Cancer of the Cervix". This meeting was followed by a convocation at which the newly admitted Fellows were presented and an honorary fellowship was awarded to Sir Harry Platt, President of the Royal College of Surgeons of England. On Saturday evening the President's reception was followed by the annual dinner, at which the guest speaker was the Abbé Arthur Maheux of Quebec.

Association Notes

EXECUTIVE COMMITTEE MEETING

The regular fall meeting of the Executive Committee of the Canadian Medical Association was held on Friday and Saturday, November 11 and 12. This meeting was an historic occasion since it was the first to be held in the new home of the Association at 150 St. George Street, Toronto. Although the secretarial and editorial offices were not transferred to this building until November 21, the new board room had been prepared ahead of time so that the Committee might enjoy the amenities of their own new home. Members of the Committee toured the new building and their comments on this were entirely favourable. As before, we are publishing some of the features of this meeting which may be considered of fairly wide interest to readers of this journal.

The President, Dr. T. C. Routley, gave a report of his visits to the divisional annual meetings, in which he mentioned that the same problems had been encountered with variations in all provinces. Problems to be faced included those in the fields of medical care, hospitalization, public relations, medical economics and medical ethics. The delegates to the Vienna Assembly of the World Medical Association reported to the Committee; after hearing the delegates' report and discussing it, the Executive Committee adopted a resolution recommending that the C.M.A. Special Committee on International Relations be reconstituted as a Standing Committee on International Relations and the World Medical Association, with a chairman, local nucleus and corresponding members for divisions. It is unnecessary to repeat here the material of the report of the World Medical Association Assembly since Dr. Kirk Lyon has prepared a special report (see page 904). The 1959 W.M.A. Assembly is to be held in Canada, following the World Conference on Medical Education in Chicago. It is expected that the Assembly will take place in the Province of Quebec.

The President-elect, Dr. R. Lemieux, gave a progress report on the Annual Meeting, 1956. The picture presented was most attractive, and it was clear that the local committees in Quebec had got their preparations to an advanced stage. A number of social attractions are planned, in addition to a full and varied scientific programme. It is expected that at this, the first meeting in Quebec City in 30 years, the Osler oration will be given by a French physician sent over by his government. Scientific meetings will be held at the Ecole de Commerce, which, in the words of our President-elect, "might have been built for a C.M.A. meeting". Because of the very satisfactory facilities, it is hoped to make the scientific exhibition this year a much bigger and more important feature of the meeting than usual.

Mr. L. W. Holmes reported on public relations activities of the C.M.A. He listed these activities under three principal headings: information and education, fact finding and integration. The most interesting feature under the first heading was a booklet entitled "You and the C.M.A." of which a 12-page dummy was available for inspection. This coloured booklet which is addressed both to the membership and the potential membership of the C.M.A., will be available in English and French and is designed to acquaint readers of the structure, function and services of the C.M.A. Its appearance was favourably commented on by the Executive Committee, and plans for printing and distribution are proceeding. Mr. Holmes also discussed his work in relation to press, radio, television and other educational activities. He is still continuing his visits to divisions of the Association in order to study current public relations activities, to discuss specific problems, to make suggestions for integration of divisional programmes and to meet with press, radio and TV personnel.

It will be recalled that the report of the Committee on Ethics to Council in June was referred back to the Committee for further study of certain proposed amendments. The amended report was discussed and finalized by the Executive Committee, as was the amended Basis of Approval of Hospitals for the Training of Interns in Canada which had similarly been referred back in June. As regards the latter document, which was presented to the Committee by Dr. Gilbert Turner of Montreal, the Executive Committee after discussion approved the final version which will be printed and distributed to hospitals across Canada with an invitation to them to apply for approval as training institutes for interns. It is expected that the relevant committee will have to meet next year to consider these applications.

The Committee welcomed Dr. Harold Elliott of Montreal who submitted the report of the new Committee on Traffic Accidents. He informed the Executive Committee of the recommendations of the Montreal conference on Medical Aspects of Traffic Accidents, held last May. These were: (1) that a national institute for medical research in traffic accidents be set up; (2) that the proceedings of the conference be published; (3) that an annual forum be held in other large cities, similar to the Montreal conference. After considerable discussion the Executive Committee adopted a resolution approving in principle the setting up of a national institute for medical research in traffic accidents, asking Dr. Elliott's committee to study the matter further and to be prepared to hold a conference at the time of the next Committee meeting to examine the proposal in detail. In the meantime the Executive suggested that the opinions of the divisions be sought on this subject.

Dr. R. M. Parsons of Red Deer, Alberta, presented the report of the Special Committee on Pensions of the Permanently and Totally Disabled. This report was the result of consultations with divisional secretaries and Dr. K. C. Charron, the key federal official in this field. Administration of this new programme, which started in provinces between January 1 and April 1, 1955, appears to be proceeding better than at the start, though the screening of individual applicants for pensions varies greatly from province to province. In one province, for example, over 70% of applicants were found suitable for a disability pension, whereas in others the figure was very low. The Executive Committee discussed various features of the programme as it affected doctors and it is expected that their comments will be taken into account when the programme is reviewed at the end of a year of operation.

There were four applications for affiliation under Section VII-1a of the By-Laws. The Executive Committee will recommend to Council that the following bodies be admitted to affiliation: The Canadian Association of Pathologists, the Canadian Association of Physical Medicine and Rehabilitation, the Canadian Ophthalmological Society and the Society of Obstetricians and Gynæcologists of Canada. The Executive Committee supported the suggestion, coming from the Canadian Heart Association, that a Canadian Heart Foundation would be desirable, since this is the only major area in medicine which is not the concern of a medico-lay body. It is hoped that a conference will be called by the Minister of National Health and Welfare early next year with a view to establishing such a foundation.

Trans-Canada Medical Plans had submitted a memorandum to the Executive Committee proposing the development of an economic research bureau for the joint use of T.C.M.P. and the C.M.A. and its provincial divisions. Such a research bureau should be able to furnish a great deal of information on medical economics, which is not now readily available to the organized medical profession. The Executive Committee decided to support the establishment of such a bureau and provision has been made in the 1956 budget for financial assistance.

The General Secretary of the C.M.A. read to the Executive Committee an invitation to be represented at the 32nd All-India Medical Conference in Jaipur, December 26-28, 1955. He said that this was one of the many invitations received and the Committee agreed that in future invitations of this nature would be printed in the *C.M.A.J.* so that Canadian doctors who might find themselves in the vicinity of such conferences could possibly arrange to represent the C.M.A. at such gatherings.

The Executive Committee accepted the gracious invitation of the American Medical Association to hold the midwinter conference of divisional secretaries at the A.M.A. Headquarters in Chicago, probably on February 15 and 16. The Committee also heard with pleasure that the Association des Médecins de Langue Française du Canada had nominated Dr. J. E. Dorion, Quebec, Dr. Pierre Jobin, Quebec, and Dr. Y. Rolland Blais, Montreal, as their delegates on the Committee on Economics.

The next meeting of the Executive Committee will take place at 150 St. George Street on Friday and Saturday, March 16 and 17, 1956.

CORRESPONDENCE

BARBITURATE AND MORPHINE ANTAGONISTS

To the Editor:

It was most informative to read Dr. Harris's comments on our letter (*Canad. M. A. J.*, 73: 498, 1955).

We do not wish to create a controversy when so little is known about the actual mode of action of Megimide and Daptazole. However, it is desirable to record that our original six cases were those of simple barbiturate anæsthesia and not massive dosage. We used the dose as recommended by the manufacturer and as used by Harris,[1] and in certain instances, much larger doses, although we did not give the drug as rapidly as Harris suggested in his letter.

We have, since reading Dr. Harris's letter, given the doses at a rapid rate with improvement in our results. Unfortunately, in one case, where Megimide and Daptazole were used in this manner, convulsions occurred. Our results, along with the manufacturer's warning concerning the possibility of convulsions, still leave us with the belief that Megimide is akin to the analeptics. A recent personal communication from the manufacturer stated that "at a recent meeting there was no agreement amongst investigators as to the mode of action, dose or value of Megimide."

J. T. Wright,[2] commenting on the article by Shulman *et al.*,[3] refers to Megimide and Daptazole as "having analeptic activity, especially where short-acting barbiturates are concerned." He adds, "there is doubt about a 'safe state' bordering on convulsions, and it is suggested that specific antagonism should be proved in the case of the long-acting barbiturates."

As we have observed one convulsion and one prolonged coma in a very small series, we feel that our original word of caution was justified, and until more is learned about these drugs enthusiastic comment should be withheld. It is possible that Megimide and Daptazole will allow for their safe use in barbiturate and morphine antagonism, but only when extensive biochemical and clinical investigations have been carried out.

E. A. GAIN, M.D., AND
S. G. PALETZ, M.D.

Dept. of Anæsthesia,
University of Alberta Hospital,
Edmonton, Alberta,
October 26, 1955.

REFERENCES

1. HARRIS, T. A. B.: *Lancet*, 1: 181, 1955.
2. WRIGHT, J. T.: *Ibid.*, 1: 1329, 1955.
3. SHULMAN, A. *et al.*: *Brit. M. J.*, 1: 1238, 1955.

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BARBITURATE ANTAGONISTS

To the Editor:

I was most interested to read the correspondence, in your issue of September 15, concerning Megimide.

Since the *Lancet* published Harris's article, I have followed the correspondence on this drug and note that, whilst most comments are favourable, they refer to the use of Megimide in the reversal of barbiturate poisoning.

Harris reported most success in the group given short anæsthesia and no premedication but did not discuss barbiturate poisoning successes. Few other workers have reported the use of Megimide as a means of shortening sleep following clinical anæsthesia.

I should like to record my agreement with the findings of Gain and Paletz. At the time of publication of Harris's paper, I was conducting an investigation (as yet unpublished) comparing the safety of local and general anæsthesia for bronchoscopy. It was considered important that the patient should be awake (i.e. able to converse) immediately following the examination, and a small series of cases was given Megimide with this in mind. In no case did the patient wake "on the end of the needle" and I was forced to abandon the use of the drug as it appeared to serve no useful purpose. Megimide was given in accordance with the method described by Harris. The patients had received premedication with Pantopon and hyoscine and were anæsthetized with thiopentone mg. 500 and succinylcholine. No inhalation agent was given.

A few patients showed signs of "stimulation", e.g. hyperpnœa and movement, which were not maintained more than a few minutes.

At the time, I communicated my findings to Messrs. Nicholas Products Ltd., who had very kindly supplied the Megimide, and they replied that this was the first adverse report they had received.

One must conclude that this agent is of value in reducing the depth of depression in barbiturate poisoning, especially when combined with Daptazole, but my small experience suggests that it would not raise a patient from "first plane" to consciousness, should this be required following clinical anæsthesia, e.g. in a patient with severe respiratory disease.

H. BARRIE FAIRLEY, F.F.A.R.C.S.

Toronto General Hospital,
Toronto, Ont.,
October 11, 1955.

PETHIDINE ADDICTION

To the Editor:

I have received the following communication from the Director-General of the World Health Organization, Geneva, Switzerland, in relation to the drug pethidine:

"The Expert Committee on Drugs Liable to Produce Addiction, at its fifth session (World Health Organization Technical Report Series 95, p. 10, section 7.3.2), having considered a report on pethidine addiction as encountered at the Public Health Service Hospital, Lexington, Kentucky, U.S.A., and noting the high incidence of such addiction among members of the medical, nursing and associated professions, considered that an important factor in the development of pethidine addiction not only in the United States of America but also in other countries has been the attitude of physicians towards the drug, based upon the widespread belief that it is less dangerous in this respect than morphine.

"Being convinced that experience with the drug, both in experiments and in clinical practice, is contrary to this belief, the Expert Committee was of the opinion that pethidine is as dangerous as morphine as a potential addicting agent, that its use should be undertaken only with full realization of this danger, and that its administration should be approached with the same attitude and attended by the same precautions as are recognized for morphine, and therefore urged that the Director-General, by whatever means he might deem appropriate, bring to the attention of governments and the medical professions throughout the world the dangerousness of the addiction potentiality of pethidine and the need for the same care in its use as with morphine.

"The Executive Board of the World Health Organization, having adopted at its fifteenth session the above fifth report of the Expert Committee on Drugs Liable to Produce Addiction, I have the honour to bring to your particular notice the opinion of this Expert Committee on the dangerousness of the addiction potentiality of pethidine."

As you are no doubt aware, pethidine is the international non-proprietary name for Demerol.

K. C. HOSSICK,
Chief, Division of Narcotic Control,
Dept. of National Health & Welfare,
Ottawa.

SPECIAL CORRESPONDENCE

The London Letter

(From our own correspondent)

THE MINISTER AND GENERAL PRACTITIONERS

The Minister of Health has made yet another of his speeches in praise of family doctors. This time his plea was for more part-time hospital appointments for general practitioners. He also appealed for closer co-operation between family doctors and hospital consultants. The former should be encouraged to visit their own patients while in hospital, and they should be invited to hospital clinical meetings. Further development was also required of the x-ray and pathological services provided by hospitals for general practitioners. The Minister also asked for closer co-operation between medical officers of health and family doctors, though perhaps what was required in the first instance was closer co-ordination of the domiciliary, health and welfare activities of the local authorities themselves. If such co-ordination could be achieved, and the general practitioner could also be integrated into the scheme of things, then, the Minister felt, the general practitioner would be able to fulfil his primary function of being a family doctor. Such functional integration of the various branches of the National Health Service is long overdue. The trouble is that the bureaucratic mind, whether in Whitehall or the local town hall, finds it so difficult to understand how such integration can be achieved without masses of new rules and the accompanying torrent of paper.

HOSPITALS AND THE PRESS

Agreement has been reached at a conference of doctors and representatives of the press, held under the auspices of the British Medical Association, on the procedure which it is recommended should be adopted in hospitals for the release of news about the condition of patients. No information should be divulged to the press without the consent of the patient, beyond the admission on enquiry that the person concerned is a patient. Where, however, even this statement would be deleterious to the patient's interests, his presence in the hospital should not be disclosed without his consent: e.g., in certain special hospitals, such as mental hospitals, where the mere admission of the patient implies

the nature of the diagnosis. In the case of well-known people, and subject always to the patient's consent, a brief indication of progress may be given, in terms authorized by the doctor in charge. The procedure recommended in the case of accident cases depends on whether one or more cases are concerned. In individual cases the press should be given, on enquiry only, and at the time of the enquiry or as soon as possible afterwards, the name and address of the patient and a general indication of his condition. In multiple accident cases (e.g., a railway accident) all reasonable steps should be taken to inform relatives of the injured before the publication of names, bearing in mind the necessity of early publication to dispel the anxiety of next-of-kin of all other persons who might have been involved in the accident. To facilitate all such arrangements it is recommended that all hospitals should ensure that a sufficiently senior and responsible officer of the hospital is at all times available to answer press enquiries, and should nominate an officer or officers for this purpose. All eight recommendations of this conference are admirable in intent and in content, but all are dependent upon the preamble to the eighth recommendation: "Co-operation between hospitals and the press must depend on mutual confidence and good personal relations". If these are present, no rules are necessary; if they are lacking, no amount of rules will help either the hospital or the press.

Family Help Service

Details have just been released of a most interesting experiment in child welfare. On April 1, the medical officer of health for Kent introduced a "family help service". The aim of this service was to provide for the care of children in their own homes while the mother was unable to manage the household for a temporary period, usually because of illness or confinement. The procedure is that applications for help are made to the medical officer of health by the children's officer. A health worker and the domestic help organizer then visit the home to find out exactly what is needed. The latter then arranges for one of her staff to take charge of the home while the mother is away. So far, 105 families, involving 380 children, have been helped in this way, and in four out of five cases the scheme has been wholly successful. In the remainder, mainly problem families, there have been difficulties, but in only 7% of the total number of families have these difficulties been so great that it has proved difficult to find a helper who was prepared to take on the job. Financially the scheme is undoubtedly a success; so far the cost of the scheme is about half what it would have cost to take into care the children who have been looked after at home. Socially the benefits may not be so easy to assess at this stage, but there seems little doubt the keeping of the children at home and the beneficial effect of the domestic helper on the standard of the home have proved well worth while.

Neutralizing Smog

In conjunction with St. Bartholomew's Hospital the Department of Scientific and Industrial Research is carrying out an investigation into the practical possibility of neutralizing the irritant effects of fog due to their acid content. The method is simplicity itself: the releasing of small quantities of ammonia to neutralize the sulphurous acids in the air. Selected outpatients, and members of the staff, at St. Bartholomew's Hospital, are being issued with a bottle containing a solution of ammonia and a wick, which can be pulled up and the ammonia released into the atmosphere of the room. To balance the output of ammonia and the acidity of the air, a special "litmus" paper has been developed. This turns red if the atmosphere is too acid, and blue if too alkaline (i.e. too much ammonia). The correct balance is shown by the paper turning greenish-yellow.

London, November 1955 — William A. R. Thomson

ABSTRACTS *from current literature*

MEDICINE

The Problem of the Tuberculous Psychotic.

Pollak, M. and Williams, J. H: Am. Rev. Tuberc., 72: 107, 1955.

Numerous surveys conducted during the past 20 years have furnished adequate proof of the old observation that tuberculosis is an important problem among hospitalized psychotics. As a result, chest roentgenography on the admission of the patients to hospital, and at regular intervals during their residence, has become a routine procedure in progressive mental hospitals.

This study is an attempt to determine the magnitude of the tuberculosis problem in the Veterans Administration Hospital at Downey, Illinois. An effort was made to evaluate the prevalence of active tuberculosis among patients admitted for treatment of a mental disorder, and the prevalence and incidence of active tuberculosis among hospitalized psychotic patients, as well as the effect of shock therapy on the incidence of tuberculosis.

The prevalence of unsuspected active tuberculosis among male white patients admitted to a mental institution was not significantly different from prevalence rates obtained in investigation of patients admitted to general hospitals. The prevalence of tuberculosis among male white mental patients was much higher among patients over 45 years of age than it was among patients between 20 and 45.

The incidence of active tuberculosis among male white psychotic patients with no history of tuberculosis was 5.7 per 1,000 person-years. Among male white psychotic patients with previously inactive or arrested tuberculosis, the rate was 31.1 per 1,000 person-years. There is an obvious need for close surveillance of those patients with inactive or arrested tuberculosis.

Despite an active case-finding programme, one-sixth of the tuberculosis cases discovered among the psychotic patients were detected only after the appearance of clinical symptoms. No evidence was found to indicate that use of shock therapy resulted in an increase in the incidence of tuberculosis. S. J. Shane

Sarcoidosis; An Analysis of Twenty-one Proved Cases.

Finestone, A. W.: Am. J. Roentgenol., 74: 455, 1955.

A study is presented of 21 cases of proven sarcoidosis seen at the Jefferson Hospital, Philadelphia, over a five-year period (1947 to 1952). The findings were similar to those previously reported by other authors. The most common symptoms were dyspnœa (nine cases) and cough (eight cases). Four patients complained of joint pains and weight loss and one of fatigue. Four were asymptomatic. Physical signs in the 21 cases were peripheral adenopathy (ten), skin changes (five), hepatomegaly (four) and splenomegaly (one). Radiological abnormalities in the group were as follows: enlargement of mediastinal nodes (35%); positive changes in the lungs (25%); mediastinal node enlargement with positive lung changes (40%).

These patients had been followed up for from two weeks to five years; eleven were well, five were complaining of dyspnœa, two were unimproved, one had a complicating active tuberculosis and two patients were dead. Death resulted from carcinoma of the gallbladder in one case and from histoplasmosis in the other.

This study reaffirms the essentially benign nature of sarcoidosis. The age of onset is usually between 20 and 30 years, the course is chronic and relapsing, symptoms are frequently absent and are mild if present, the diagnosis

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can usually be suspected from abnormalities present in the radiograph of the chest and can be confirmed in a high percentage of cases by biopsy of liver, lung or tonsils. The serum total protein and globulin are above normal in amount in one-third of cases.

NORMAN S. SKINNER

SURGERY

Review of Post-mortem Examinations in Combat Casualties.

STRAWITZ, J. G. ET AL.: A.M.A. ARCH. SURG., 70: 260, 1955.

The authors, members of the Surgical Shock Research Team in Korea, review autopsy findings. Petechial hæmorrhages involving the serous and mucous membrane surfaces were common. Gross congestion of all organs and striated muscles with weeping from the cut surface were salient observations. Microscopic evidence of dilatation of all blood vessels would be seen as an indication of markedly increased vascular bed.

This study suggested that the pulmonary œdema which has been considered a constant and integral part of the pathogenesis of shock probably follows shock and transfusion rather than ischæmia alone. Irreversible shock, vital organ damage and uncontrolled hæmorrhage constituted the major causes of death, but often many other factors were at play. Renal damage, with hemecasts within the tubules as well as varying degrees of tubular epithelial degeneration, was common.

Fat emboli were present in more than 90% of men dying of battle wounds but as a causative factor were uncommon. Occasionally they were demonstrable in the kidneys. Strict criteria were followed to differentiate this as an incidental finding from the primary cause of death.

ALLAN M. DAVIDSON

The Effect of Severe Battle Injury and of Post-traumatic Renal Failure on Resistance to Infection.

BALCH, H. H.: ANN. SURG., 142: 145, 1955.

The author, as a member of the Surgical Research Team in Korea, carried out this study to investigate the antibacterial defence systems in a group of severely wounded casualties with and without post-traumatic renal insufficiency. The phagocytic activity of the circulating leukocytes, the body's capacity to synthesize specific antibodies, and the plasma complement level in patients were all assessed and correlated with other clinical data.

There was no definite evidence that the phagocytic activity was related to any of the changes in plasma chemistry and indeed was sometimes not depressed even in cases of severe uræmia. However, a significant depression in the neutrophil activity was found within the first 24 hours after several patients were wounded and was the only abnormality noted in the antibacterial defence mechanism studied. It however returned to normal within 48 hours.

It is concluded that battle casualties with or without renal insufficiency are no more likely to develop infection because of defective antibacterial defence mechanisms. On the other hand, factors of paramount importance include nature and extent of trauma and bacterial contamination, length of time from injury to initial operation and adequacy of debridement.

ALLAN M. DAVIDSON

Injuries of the Liver.

MADDING, G. F.: A.M.A. ARCH. SURG., 70: 748, 1955.

When there is doubt regarding the presence of a ruptured viscus and the patient is not improving, exploration is indicated. Shock should be treated by transfusions, but autotransfusion is contraindicated in ruptured liver because of the presence of bile. Surgical treatment of all diagnosed liver wounds is recommended, for delay increases the risk and infection is common, even though spontaneous hæmostasis is noted in 91%. At operation all loose blood and clots and devitalized liver tissue are removed. The use of gelatin sponge and oxidized cellulose is not approved, and individual transfixion-ligation of bile ducts and bleeding vessels is recommended. Adequate drainage is important and rubber tubes are preferred to gauze packs. Such drains should be removed slowly by daily shortening. Antibiotics are used routinely but do not prevent the complications which follow inadequate drainage.

BURNS PLEWES

Carcinoma of the Thyroid and Other Diseases of the Thyroid in Identical Twins.

ROBINSON, D. W. AND ORR, T. G.: A.M.A. ARCH. SURG., 70: 923, 1955.

The authors report three pairs of identical twins each with twin lesions of the thyroid gland; carcinoma, nontoxic nodular goitre and exophthalmic goitre. As a result of their researches they conclude that if disease of the thyroid develops in one of the monozygotic twins, it may be expected to develop in the other at the same or some future time. If one such twin develops carcinoma of the thyroid, the other twin should have his thyroid explored even if no signs or symptoms are present.

BURNS PLEWES

New Physiologic Concepts Related to the Surgical Treatment of Duodenal Ulcer by Vagotomy and Gastroenterostomy.

OBERHELMAN, H. A. JR. AND DRAGSTEDT, L. R.: SURG., GYNEC. & OBST., 101: 194, 1955.

Evidence has previously been presented to show that duodenal ulcers are usually caused by a hypersecretion of gastric juice of nervous origin, whereas gastric ulcers are usually due to a hypersecretion of gastric juice of hormonal origin. The latter is thought to be mediated by the antrum of the stomach, which acts as an endocrine organ and releases gastrin in response to certain food and other stimuli. An excessive secretion of gastric juice of hormonal origin may be due to prolonged contact of food with the antrum mucosa where there is associated hyperperistalsis, hypermotility or pyloric stenosis.

Experimental surgery on dogs suggests the explanation of some of the unsatisfactory results of vagotomy for ulcers in man. It appears that division of the vagus nerves markedly stimulates the release of gastrin from the antrum, in response to stasis of food in the gastric antrum, due to a decrease in the tonus and motility of the stomach as a result of the vagotomy. Where stasis of the food was prevented in the animal by a gastro-enterostomy placed in the gastric antrum, or where the antrum had previously been resected, the hypersecretion of gastric juice did not occur. Presumably the responsible hormonal agent is gastrin.

An analysis is made of 158 patients who were treated for duodenal ulcer by vagotomy alone. This is compared with a group of 487 patients treated by vagotomy plus gastro-enterostomy. Failures were usually due to stasis of food in the stomach and a high-lying gastro-enterostomy. Experimental and clinical evidence indicates that wherever a gastro-enterostomy is done along with a vagotomy for duodenal ulcer, the stoma should be placed in the antrum 4 or 5 cm. from the pylorus.

A. D. POLLOCK

OBSTETRICS AND GYNÆCOLOGY

Triethylene Melamine in the Management of Far Advanced Ovarian Cancer.

SYKES, M. P. ET AL.: SURG., GYNEC. & OBST., 101: 133, 1955.

Twenty-six patients with far-advanced and inoperable recurrent ovarian cancer were treated with triethylene melamine (TEM). Fourteen obtained some degree of symptomatic improvement, and of this group eight showed objective evidence of tumour regression. The usual duration of treatment ranged from one to three months. One patient benefited for 11 months and another has now shown no evidence of recurrent disease for a period of four years. The latter case may represent a spontaneous remission. On the basis of these observed responses, an adequate trial of TEM or a related compound is indicated in patients with a non-resectable or recurrent ovarian cancer. TEM may precede, follow, or be administered concurrently with x-ray therapy. ROSS MITCHELL

Rapid Determination of Plasma Fibrinogen.

GLENDENING, M. B., OLSON, L. AND PAGE, E. W.: AM. J. OBST. & GYNEC., 70: 655, 1955.

A procedure for determination of plasma fibrinogen, accurate within a standard error of 17 mg. %, has been developed specially for cases of severe abruptio placentæ. Results can be reported within 30 to 45 minutes from the time a request is made. The method is based on a determination of the moist weight of a fibrin clot and the use of an equation for converting this weight to plasma concentration. ROSS MITCHELL

Endometriosis of the Cervix Uteri.

WILLIAMS, G. A. AND RICHARDSON, A. C.: OBST. & GYNEC., 6: 309, 1955.

Forty-two cases of endometriosis of the cervix from the literature are reviewed and 35 new cases presented. Endometriosis of the cervix is probably not as uncommon as is generally assumed. It can be diagnosed readily at the time of the onset of the menstrual flow or shortly thereafter.

The disease *per se* is of trivial importance, but may produce alarming symptoms and occasionally presents a disturbing appearance which must be differentiated from malignancy. Trauma to the cervix is probably an etiological factor, only one patient in this series being exempt. The incidence of primary and secondary sterility and of spontaneous abortions among these patients is relatively high. Cervical endometriosis is usually successfully treated by light cauterization or fulguration.

An extremely high incidence of decidual reaction in the cervix in patients who subsequently become pregnant suggests a causal relationship, but this cannot be established in any case. ROSS MITCHELL

Urethral Trichomoniasis in the Female.

KEAN, B. H.: AM. J. OBST. & GYNEC., 70: 397, 1955.

Of 45 patients with *Trichomonas vaginalis* infections, 38 had parasites in the vagina and 40 had parasites in the urethra; 33 had parasites in the vagina and in the urethra, 5 had parasites only in the vagina, and 7 had parasites only in the urethra. In many instances, when parasites were present both in the vagina and the urethra, they were more numerous in the urethra. This localization of *Trichomonas vaginalis* in the urethra may be an important factor, responsible for recurrence of *T. vaginalis* vaginitis.

Case reports suggest a relationship between *T. vaginalis* vaginitis and recurrent cystitis caused by *Escherichia coli* and other bacteria. It is possible that bacteria are transported to the bladder by *T. vaginalis*. ROSS MITCHELL

Management of Persistent Brow Presentation.

MOORE, E. J. T. AND DENNEN, E. H.: OBST. & GYNEC., 6: 186, 1955.

The incidence of persistent brow presentation is 0.14%. In the series under review brow presentation occurred with equal frequency in primiparas and multiparas, and delivery was spontaneous in only 11%. Conversion to a vertex or face presentation is more apt to be successful by instrumental means than by manual technique. Forceps delivery should be attempted only when all the prerequisites have been satisfied. High forceps must be avoided. Version should be attempted only by the experienced operator and then only when circumstances are favourable.

Cæsarean section is usually the best method of delivery for the elderly primipara and for those cases in which any difficulty is encountered in the management of labour or delivery. ROSS MITCHELL

Placenta Prævia: A Review of 200 Cases.

GRANT, F. G.: J. OBST. & GYNÆC. BRIT. EMP., 72: 497, 1955.

In the period 1946-1953, 200 patients were admitted to the Royal Maternity Hospital, Belfast. The management of these patients followed closely the principles outlined by Macafee. In the patients who were admitted at an early stage of pregnancy every effort was made to prolong the pregnancy to the 37th or 38th week, provided this did not jeopardize the safety of the mother.

In the series, 201 infants were delivered and of these 10 were stillborn and 14 died in the neonatal period, a gross fetal mortality of 11.9%. This compares favourably with the fetal mortality of 56.3% from placenta prævia cases in the series between 1932 and 1935.

The five factors which contributed to these results are: (1) the co-operation of general practitioners and midwives in not making vaginal examinations prior to admission to hospital; (2) conservative treatment where the infant was unduly premature; (3) the extended use of Cæsarean section for delivery, especially in those patients with major degrees of placenta praevia; (4) the great improvement in blood transfusion service; (5) the very great help afforded by the pædiatric service. ROSS MITCHELL

PÆDIATRICS

Milk Drip via an Indwelling Naso-Gastric Rubber Tube for Feeding Premature Infants.

HOLMDAHL, K.: ACTA PÆDIAT., 44: 330, 1955.

The use of an indwelling soft rubber catheter, to supply milk in continuous drip to premature babies, has been found to decrease the incidence of vomiting and asphyxial attacks resulting from overdistension of the stomach. Attacks of cyanosis occur in about the same proportion of children as when ordinary gavage is used. In the author's experience, there was a distinct lowering of the death-rate, from 18.1 to 12.9%. Disturbance to the infant is slight, irritation of the mucous membranes negligible, and more food can be administered during a 24-hour period. Less time and less-skilled assistance are required. I. J. PATTON

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Etiology of Cerebral Palsy: An Experimental Approach.

DENHOFF, E. AND HOLDEN, R. H.: AM. J. OBST. & GYNEC., 70: 274, 1955.

A study of possible causative factors in cerebral palsy was made with 15 children who had "suspicious" findings of brain damage at birth and neonatally, and 17 healthy controls selected as a random sample from 504 consecutive ward births.

Only four (27%) of the "suspicious" group had abnormalities in physical, psychological and/or social development when intensively studied after 2½ years. Three (18%) of the control group had similar findings. The only factor common to the deviantly developed children in *both* groups was a history of previous abortion in the mother.

It is concluded that one important area of research in the etiology of cerebral palsy involves further investigation of reproductive physiology.

ROSS MITCHELL

Effect on the Newborn Infant of Reserpine Administered Ante Partum.

BUDNICK, S., LEIKIN, S. AND HOECK, L. E.: A.M.A. AM. J. DIS. CHILD., 90: 286, 1955.

The use of rauwolfia preparations, such as reserpine, for the treatment of hypertension associated with the toxæmia of pregnancy, may have undesirable effects on the baby. Nasal discharge was observed shortly after birth in 12 infants whose mothers had been so treated, an incidence of 16%.

One other baby, whose mother had received no reserpine, had a nasal discharge, but the clinical course was very mild, unlike that of the other 12.

These showed obstructive signs with retraction, and with cyanosis in the more severe cases. Secondary developments, which occurred in several, included pulmonary congestion, lethargy, and difficulty in feeding. The toxic reaction lasted one to five days. Oxygen, and use of the prone Trendelenburg position, seemed to be the only effective treatment. There were two deaths.

I. J. PATTON

THERAPEUTICS

An Evaluation of the Effect of Continuous Long-Term Anticoagulant Therapy on the Prognosis of Myocardial Infarction.

SUZMAN, M. M., RUSKIN, H. D. AND GOLDBERG, B.: CIRCULATION, 12: 338, 1955.

Two hundred and eight patients with myocardial infarction, having received anticoagulant therapy during the acute phase and having survived for three months or more, were observed 3 to 76 months until death or the end of this study (Sept. 1, 1953). Those patients treated for three months or longer comprised the long-term group while those treated for less than three months comprised the short-term control group; 120 patients were treated for three months or longer, but 38 of them who discontinued treatment after this period of time or who were treated intermittently were excluded from the comparative study. The long- and short-term groups were compared in respect of mortality, incidence of recurrent infarction, angina and cardiac failure.

In the 82 patients who constituted the long-term group the mortality rate was 7.3% and there were seven recurrences of myocardial infarction, whereas in the 88 patients in the short-term group the mortality rate was 33% and there were 24 recurrences.

Separate comparisons were made of mild and severe cases; when the former were eliminated, the mortality rate in the long-term group, which comprised 67 patients, was 9% with seven recurrences of infarction, whereas in the short-term group totalling 60 patients it was 46.7% with 21 recurrences.

Of the severe cases with a history of previous infarction, the mortality rate in the long-term group (21 cases) was 14.3% compared with 66.6% for the short-term group (15 cases).

The incidence of angina after the presenting attack of myocardial infarction was approximately the same for both groups, whereas relief or improvement of this condition occurred in 56% of the long-term group and in 23% of the short-term group.

During the course of the study cardiac failure occurred with similar frequency in both groups but the mortality associated with this complication was 11.8% in the long-term group compared with 57.1% in the short-term group.

From this study it would appear that patients in whom the presenting attack is mild in addition to being the first one, and who receive short-term anticoagulant therapy, have a favourable outlook in respect of subsequent infarction, cardiac failure and death, irrespective of whether or not the anticoagulant therapy is continued indefinitely. By contrast, the patients most likely to benefit from long-term anticoagulant therapy are those in whom not only is the presenting attack severe but there is also a history of previous myocardial infarction.

S. J. SHANE

Vena Cava Inferior Ligation in Congestive Heart Failure: Report on 100 Cases in Five Years.

BERNATH, J. *et al.*: AM. HEART J., 50: 112, 1955.

Between 1949 and 1953, 100 patients with intractable congestive heart failure were treated by inferior vena cava ligation at the Medico-chirurgical Centre of Broussais, France. The writers report their follow-up observations on these cases, after a lapse of one to five years. The patients were arbitrarily placed in five categories, including: (1) complete cardiac insufficiency; (2) mitral cardiopathy with right ventricular insufficiency and repeated emboli; (3) mitral cardiopathy with predominating pulmonary side-effects; (4) right ventricular failure of a particular type; and (5) left ventricular insufficiency.

The operation is performed under various types and combinations of anæsthesia, and is now carried out transperitoneally rather than retroperitoneally, an approach which was used in the earlier cases. Careful preoperative preparation, particularly from the standpoint of cardiac therapy, appears to be essential.

It appears to be quite clear that in those patients who survive surgery, improvement occurs immediately after operation and is highly dramatic. The most outstanding feature of this improvement is the disappearance of orthopnœa and paroxysmal nocturnal dyspnœa. However, there are frequent postoperative complications, including œdema of the lower extremities, and this type of surgery appears to be of no value in patients in whom the cardiac lesion is progressive. There is a high mortality rate during operation (13%), and an even higher mortality during the first postoperative year (23%). However, these figures decrease considerably during the second and subsequent years. For example, the survival rate after the first year is 60%, after the second 49%, after the third 40%, and after the fourth and fifth years 33%.

The authors feel, however, that the functional improvement achieved and the prolongation of life obtained justify the operative and postoperative risks to the patients.

S. J. SHANE

OBITUARIES

DR. MALCOLM H. V. CAMERON, 78, suffered a heart attack at his home in Toronto on October 31, and died in an ambulance en route to St. Michael's, the hospital which he had served for 50 years. He had been on the active staff of St. Michael's for 22 years, but continued there in the capacity of consultant surgeon after his retirement in 1930.

Dr. Cameron was born in Bruce county, near Walkerton, Ont., attended Woodstock Collegiate Institute, and graduated in medicine from the University of Toronto in 1905. He was active at the University as editor of the *Varsity* and secretary of the Students' Union, and later became a member of the Senate of the University for 20 years. Although his reputation was established mainly on his work in surgery and geriatrics, Dr. Cameron was also well known for his contribution to medical literature. He was a correspondent for the *Lancet* and the *British Medical Journal*, and was a former editor of the *Academy of Medicine Bulletin*. He was a fellow of the Royal College of Surgeons and the American College of Surgeons, and a former president of the Toronto Academy of Medicine, the Canadian Association of Clinical Surgeons, and the College of Physicians and Surgeons of Ontario.

Dr. Cameron, predeceased by his wife, is survived by three sons.

DR. MALCOLM CAMERON

AN APPRECIATION

The passing of Dr. Malcolm Cameron brings to a close the long and brilliant career of a well-loved surgeon. He was a gentle, kindly man who inspired confidence and gratitude among his patients, and respect and affection in his colleagues.

By current standards his formal education was meagre, but he had a thirst for knowledge and a love of learning that never waned, and led him to the top of his chosen profession.

He had a passion for teaching, and although ill health forced him to retire from the University staff 25 years ago, even this autumn he continued to take classes on every possible occasion, should a clinician be absent or late for an appointment. For half a century, medical students have been inspired not only by his clinical ability but also by his wisdom and graciousness. As an undergraduate he added to his income by writing a weekly column in the *Toronto Globe*, and throughout his medical career he continued to write, not only on surgical subjects but also on the history of medicine. The many papers and articles that have come from his pen attest to his scholarly mind and mastery of English prose.

His influence will continue for many years to come, not only because of the advice and instruction that he gave to so many younger men but also because they have known this humane, honest and upright man.

DR. THOMAS P. CARTER, 64, died at his home of a heart attack on October 30.

Dr. Carter was born in Schomberg, Ont. He was a graduate of the University of Toronto and was medical health officer for the town of Dundalk, Ont., where he had practised since 1921. He is survived by his widow.

DR. DONALD E. H. CLEVELAND, an internationally recognized dermatologist and a past president of the Canadian Medical Association and of the British Columbia Division, died in Vancouver General Hospital on October 22 at the age of 65. He had been in ill health for two years.

Dr. Cleveland, who was born in Victoria, had served in many important capacities in Vancouver after being on the staff of hospitals in Montreal, Manhattan and Brooklyn, N.Y. He was also active in community affairs. He studied at the University of Oregon Medical School in 1908 and obtained his degree from McGill University in 1914 before serving as a lieutenant with the British Army Medical Corps in 1916 and 1917. Later he was a captain with the Royal Canadian Army Medical Corps. Dr. Cleveland was named senior dermatologist of the Vancouver General Hospital in 1931 and served in that capacity until 1951, continuing as honorary consultant to the hospital until he retired in 1953. He was also consultant to the B.C. Cancer Institute and the provincial board of health, and a lecturer in medicine at the University of British Columbia from 1950 to 1953. He had been editor of the B.C. Cancer Bulletin since 1948, was a director of the Broadway Medical Building Co. Ltd., and had also served as senior assistant medical adviser to the Pensions Commission of Canada.

Dr. Cleveland was a Fellow of the American Academy of Dermatology, a Founding Fellow of the Pacific Dermatological Association, and a member of the British Association of Dermatologists. He was past president of many organizations, including the Canadian Medical Association, the B.C. Medical Association and the Vancouver Medical Association. He had also been president of the Catholic Doctors' Guild of Vancouver, the Association of Dermatology, and the Osler Club, which in 1953 awarded him the title "Prince of Good Fellows".

He is survived by his widow and two children, Mrs. Ivor O'Connell of Vancouver and Dr. Edward Cleveland of Winnipeg.

DR. DANIEL IRWIN DAVIS, a practising physician in Toronto for 36 years, died suddenly at his home in Willowdale during the last week of October. He was 66.

After graduating from the University of Toronto in 1916, Dr. Davis served as captain with the R.C.A.M.C. overseas in World War I. In World War II he was again with the R.C.A.M.C., serving as examining officer for troops stationed at the C.N.E.

A member of the staff of St. Joseph's Hospital, Toronto, for several years, Dr. Davis had practised privately on College and Bloor Streets. He moved to Willowdale six years ago.

He is survived by his widow and a sister.

DR. LELAND EARL GERMAN, 64, a general practitioner of Mimico, Ont., died in St. Joseph's Hospital, Toronto, on October 22 after an illness of several months.

Dr. German was born in Petrolia, Ont., and graduated in medicine from McGill University in 1924. He interrupted his studies to enlist in the Canadian Army during World War I and served overseas for four years. From 1924 to 1941, when he moved to Mimico, Dr. German was in practice in Campbellton, N.B. During World War II he served for two years as a recruiting officer.

He is survived by his widow and a daughter.

DR. J. MEREDITH GRAHAM, a general practitioner of Goderich, Ont., died in Alexandra Marine and General Hospital on October 12 after an illness of several months.

Dr. Graham was born in Ashfield Township, near Sheppardton, Ont. He served overseas in World War I with the 12th Field Ambulance from 1914 to 1919. He graduated from the University of Toronto in 1927 and interned at Harper Hospital, Detroit, and St. Mary's Hospital, Kitchener. In 1931 he went to Goderich, where he practised for 18 months with the late Dr. J. B. Whitely before taking over the practice of the late Dr. A. T. Emmerson.

Dr. Graham is survived by his widow, a son and a daughter.

DR. GEORGE W. HALL, a resident of Victoria, B.C., since 1905 and former president of the British Columbia College of Physicians and Surgeons and the B.C. Medical Association, died in St. Joseph's Hospital, Victoria, on October 1, after a long illness. He was 73. After his graduation from Trinity College, Toronto, Dr. Hall went to Victoria to open a practice with his uncle, the late Dr. Frank Hall. He retired three years ago.

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During World War I Dr. Hall went overseas with the 16th Battalion, rising to the rank of lieutenant-colonel and winning the Distinguished Service Order on the field. He was also with the army hospital service. He was an honorary member of the staffs of the Royal Jubilee and St. Joseph's hospitals and a consultant at the Wilkinson Road mental hospital.

Dr. Hall is survived by his widow and a brother.

DR. JOHN McCORVIE, a general practitioner of Peoria, Ill., died suddenly in that city on October 29. He was 64.

Dr. McCorvie was born in Chatham, Ont., and graduated in medicine from the University of Toronto in 1914. After interning at the Hospital for Sick Children, Toronto, Dr. McCorvie enlisted with the Royal Canadian Army Medical Corps and served overseas for two years. After four years with the Mayo Clinic, Dr. McCorvie received a fellowship in internal medicine and diagnosis. He subsequently set up his practice in Peoria, which he continued until his death.

He is survived by his widow and a son and daughter.

DR. WILLIAM ALEXANDER MACKENZIE, aged 81 years, died at his home at Prince William, N.B., on October 22. Dr. MacKenzie was born in Prince Edward Island, graduated in medicine from McGill University in 1903, and from that time had practised in Prince William, from which centre he served a widely spread rural population. Dr. MacKenzie had been ill for a long time but his old friends and patients continued to call on their long-time doctor to brighten his days of illness by their visits. Dr. MacKenzie was a life member of the New Brunswick Medical Society. He is survived by his widow.

DR. JOHN FREDERICK RICHES, 83, a general practitioner in Toronto for 50 years, died October 10 at Toronto Western Hospital.

Dr. Riches was born in Toronto and graduated from the University of Toronto in 1901. He was a medical referee for employment liability and insurance companies, and had retired from practice four years ago. His mother, the late Georgina Stanley Riches, principal of Sackville St. public school for 43 years, was the first woman principal in Toronto schools.

He is survived by three nephews and two nieces.

DR. HARRY GOSTICK TAYLOR, surgeon and a member of the boards of the General and Holy Cross Hospitals, Calgary, died in that city on October 22, after a short illness. He was 79.

Dr. Taylor was born in Toronto and graduated in 1904 from the University of Western Ontario Medical School. He practised for a year in Burnside, Mich., before moving to Bankhead, Alta., in 1905. In 1911 Dr. Taylor went to Calgary and had practised there until the time of his death. He served on the committee which set up the first medical association in Alberta. In June of this year he was appointed an honorary member of the Alumni Association of the University of Western Ontario.

Predeceased by his wife, Dr. Taylor is survived by a son and two daughters.

DR. WILSEY HATFIELD WHITE died at his home in Sussex, N.B., on October 3, aged 95 years. He was born in Springfield on February 16, 1860. He was a graduate of Mount Allison Academy and received his medical degree in Philadelphia, later qualifying as a dentist in Chicago. For short periods he practised in Dartmouth, N.S., and in St. Stephen, N.B. His practice in Sussex dated from 1891 for more than 50 years. Dr. White had served as a Kings County coroner and as an officer in the R.C.A.M.C. in the First World War. He was one of the last horse-and-buggy doctors in the district, and this patriarch among Maritime doctors combined medicine and dentistry throughout his active practice. He is survived by two daughters.

DR. DIGBY WHEELER

AN APPRECIATION

On September 20, 1955 there died a man known widely and favourably not only in Winnipeg and Manitoba but throughout Canada and far beyond its boundaries. On that day sometime in the early morning hours, on the train in which he and his wife were returning from a somewhat hurried but very happy visit to eastern centres, Digby Wheeler quietly dropped the threads that bound him to life.

His professional preparation was thorough and in it he very wisely laid the foundations for the wide cultural interests that figured so prominently in his later life and which not only brought great pleasure to himself but also led him into many activities that were helpful and pleasurable to others.

In his professional life he steadfastly pursued a course directed toward one objective—increased proficiency in radiology—both diagnostic and therapeutic, but medical and related fields by no means claimed his entire attention. He was a discriminating reader and while no doubt the primary recompense for this was his own enjoyment, it inevitably broadened and enriched his knowledge and did much to add to the facility in speaking that was a valuable asset in his many and varied activities.

Music was always a source of pleasure and solace to him. In it he was no dilettante. His knowledge of composers and their works was extensive and nothing pleased him more than to invite appreciative friends to listen to selections from his very large record library. These occasions were for quiet listening and desultory talk was not welcome. When the experiment of arranging weekly concerts of fine recordings for medical students was tried, he was a most enthusiastic participant.

From the time of its organization, the Winnipeg Symphony Orchestra claimed his interest. Not satisfied with being a listener he worked steadily in its support and for its welfare. During the years of his presidency it is probable that more was done to interest the community in its orchestra than ever before.

He was a most sociable person and as guest or host he could be depended upon to contribute to everyone's enjoyment, in his inimitable spontaneous fashion. His propensity for things a bit out of the ordinary—whether in clothes or motor cars—led some to think of him as something of an exhibitionist. While some small element of this sort of thing may have played a part in leading him to the display at times of the unusual, one is quite certain that he deliberately planned many of these attention-attracting things.

As a friend, he was sincere, kind and generous, never failing to respond when opportunity presented itself and often enough seeking out those whom he believed he could help. No one will ever know the number of those who were the recipients of the kind thoughtfulness of Mrs. Wheeler and him. A veritable host of witnesses could and would testify to the goodness that came to them from that home.

One may view with concern the seemingly inevitable tendency in modern society to discourage individuality and overvalue uniformity and conformity. The net result all too often is the production of monotonous mediocrity. Nowadays there seem to be few counterparts of the strong and noteworthy personalities of the not-too-remote past. Digby had about him a certain unmistakeable uniqueness. His was no life of resigned acceptance of things as they are. Being a bit different concerned him little. He enjoyed it. And this along with his many other characteristics will insure him a place in the respectful and affectionate remembrance of those who knew him.

One does not know what intimations he may have had that life would not be long and its termination sudden. If he had such, he kept them to himself and pursued his usual life unmindful of or disregarding them. One can believe that even with his zest for life and his intense interest and enjoyment of so many things, he would not have had the inevitable when it came, different from what it was.

R.M.

PROVINCIAL NEWS

SASKATCHEWAN

The Saskatchewan Research Council has recently indicated plans to build a new research laboratory on the campus of the University of Saskatchewan, according to a recent announcement in the *Star Phoenix* of Saskatoon.

During the first half of 1955 the Saskatchewan Hospital Services Plan covered 812,560 residents of the province for hospital expenses. Residents of the northern health district may voluntarily become beneficiaries.

In the six months' period the Plan paid 11,473 hospital accounts totalling nearly $9,000,000. Administration costs worked out at 3.3%, with the Plan employing 117 persons.

The Saskatchewan Division of the Canadian Cancer Society last year granted $250,000 for the construction of a medical research centre to be built on the campus of the University of Saskatchewan, and a further sum of $60,000 to provide equipment and furnishings. It was found in the study of plans that an additional $95,000 would be necessary to provide adequate space and facilities for carrying out a long-range research programme. At a meeting of the Society's executive in Regina, it was decided to provide this extra money. Upon completion of the building, the full amount contributed by the Society will total $395,000. The building is to be erected on a site opposite the University Hospital and will be connected to the hospital by a tunnel. The President, Dr. W. P. Thompson of the University, stated that it was hoped a start could be made this fall. Plans have been approved by the University Board of Governors, but tenders have not yet been called.

The Annual Convention of the Saskatchewan Division of the Canadian Medical Association in conjunction with the College of Physicians and Surgeons of Saskatchewan was held in Regina on October 17 to 21. All meetings scheduled except the Friday morning clinical session were held at the Hotel Saskatchewan, Regina. The clinical session was held at the Regina General Hospital under the chairmanship of Dr. Sid Young of Regina, those in attendance being guests of the Board of Governors of the Regina General Hospital at a noon luncheon.

The Council of the College, consisting of the representatives of the nine medical electoral districts, met on Saturday and Sunday preceding the Convention, and there was a Monday meeting of the Central Health Services Committee.

On Tuesday evening, the Annual Dinner of the College was held and Dr. T. C. Routley, President of the Canadian Medical Association, addressed those present.

The business meetings of the Association were held Tuesday and Wednesday morning with clinical sessions Tuesday and Wednesday afternoon and Thursday.

Dr. A. D. Kelly spoke at the noon luncheon on Tuesday, Mr. A. W. Embury of Regina at the Wednesday luncheon, and on Thursday the guest speaker was Premier T. C. Douglas.

The Munroe Lecture, "Surgery of the Pancreas", was delivered by Dr. Walter C. MacKenzie, Professor of Surgery, University of Alberta, Edmonton. This lectureship was arranged through the courtesy of the Saskatchewan Division of the Canadian Cancer Society in honour of Dr. Frederick D. Munroe, sometime Minister of Public Health in the Province of Saskatchewan, who in 1930 was responsible for the first legislation dealing with cancer to be introduced in a parliamentary body in the British Commonwealth. The Munroe Lecture is an annual one and is given as part of the Scientific Programme of the Convention.

Among the visiting speakers were Professor Harry Botterell of Toronto, and Dr. J. C. Beck of Montreal.

G. W. PEACOCK

MANITOBA

Dr. Alan Klass has been elected chairman of the executive committee of the Manitoba branch of the Canadian Institute of International Affairs.

Dr. Joseph Bernard Thonne has been appointed a vice-president of the International Society for Nutritional Research.

The 16-bed Wilson Memorial Hospital at Melita was formally opened on September 15 by the Honourable R. W. Bend, Minister of Health and Public Welfare. Mrs. F. C. Wilson, widow of the late Dr. Wilson for whom the hospital was named, cut the ribbon declaring the building officially open. George Franklin, representative of Manitoba Pool Elevators, presented a cheque for $3,000.

Dr. Mark Nickerson, Professor of Pharmacology and Medical Research, University of Manitoba, was the guest speaker at the annual meeting of the Multiple Sclerosis Society on September 21. Dr. A. T. Mathers gave a report from the medical advisory board.

Dr. E. L. Ross, Medical Director of the Sanatorium Board of Manitoba, recently returned from an extended tour of Great Britain and the Continent as representative of the Canadian Tuberculosis Association. Dr. Ross attended the Commonwealth Health and Tuberculosis Conference in London where he presented a paper on "X-ray and Tuberculin Surveys". He also represented Canada at a meeting of the International Union Against Tuberculosis in Paris.

Dr. D. L. Scott, Medical Superintendent of the Central Tuberculosis Clinic, attended the postgraduate course on tuberculosis of childhood, September 26-30, at the Department of Pediatrics of New York University College of Medicine, Bellevue Hospital, New York.

Dr. S. Pogonowski has been appointed to the medical staff of Clearwater Lake Sanatorium. He is a graduate of the Polish School of Medicine, Edinburgh University, and for the past three years was a medical officer for the Bahamas Government at the Princess Margaret Hospital, Nassau.

Dr. Percy Johnson of Flin Flon has been appointed president of the council of the College of Physicians and Surgeons of Manitoba. Other officers are Dr. A. E. Childe, Winnipeg, vice-president; Dr. M. T. Macfarland, registrar; and Dr. T. H. Williams, St. James, treasurer. The registrar reported that 1,016 physicians are registered (as at September 30, 1955) compared with 526 in 1945. In Greater Winnipeg there are 754 doctors practising and in rural Manitoba 262.

Dr. P. H. T. Thorlakson has been appointed president of the Alumni Association of the University of Manitoba.

Grandview will have a new hospital in March 1956. The present hospital has been condemned and a federal health grant of $29,790 will help to construct the new building. It will provide space for 17 patients, six infants and a community health centre.

Dr. John A. Hildes will leave his post as medical director of Winnipeg's municipal hospitals to join a new Arctic medical research unit at the University of Manitoba which is being set up by the Defence Research Board.

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On October 11 Dr. Stuart Schultz was elected Mayor of Brandon by acclamation.

Dr. Jack Waugh, who for eight years has been on hand to care for athletes in high school football in Winnipeg, was presented with binoculars in a pre-game ceremony on October 11. The director of school athletics in making the presentation referred to Dr. Waugh's interest in high school boys which led him to serve without remuneration.

St. Boniface council has approved fluoridation of water. Dr. Scatliff, head of the St. Boniface health unit, told council that of 825 children whom he had examined in St. Pierre where fluorine occurs naturally in the water, only 18.4% suffered tooth decay and that in the nearby town of Steinbach, without fluorine, about 71% had dental trouble. He said that about 60% of St. Boniface children examined had poor teeth. Fluoridation, he predicted, would cut these figures sharply. Winnipeg city council is still discussing the question of fluoridation of its water supply.

Dr. A. Cameron Wallace, formerly assistant professor of medical research in the University of Western Ontario, has begun his new duties as associate professor of pathology in the University of Manitoba.

On October 18, Dr. J. C. Wilt addressed the Scientific Club of Winnipeg on the virology of poliomyelitis. Dr. Wilt is chairman of the department of biochemistry and director of the virus research laboratory.

Dr. Charles F. Code, Mayo Clinic, Rochester, Minn., has been elected an honorary member of the Scientific Club of Winnipeg which celebrated its jubilee on October 28 with a dinner at the Royal Alexandra Hotel.

The fourth annual Manitoba Hospital and Nursing Conference took place October 18-20 at the Royal Alexandra Hotel, Winnipeg. Visiting doctors who took part were Dr. J. Gilbert Turner, Montreal, President of the Canadian Hospital Association; Dr. W. D. Piercey, Executive Director, Canadian Hospital Association; and Dr. H. M. Coon, Madison, Wisconsin, Trustee, American Hospital Association. The local doctors on the programme were Drs. Howard Reed, E. N. East, A. G. Rogers, Bruce Chown, F. H. Burgoyne, Paul Green, J. Hoogstraten, J. C. Wilt, J. M. Lederman, R. L. Cooke, A. R. Gordon and Paul L'Heureux.

ROSS MITCHELL

ONTARIO

Professor R. F. Farquharson presented the first of a series of lectures on geriatrics at the Baycrest Hospital for the Chronically Ill, Toronto, on September 29. Discussing the care of the aged patient, Dr. Farquharson first outlined the problems to be solved, laying stress on the importance of psychological changes, often less grave than the patient imagines. The common attitude of hopelessness in the elderly must be combated; the patient must not be allowed to think that he is too old to learn. The principles governing treatment of the aging include: (1) increasing physical rest (though this is very variable); (2) continued mental and physical activity (just as important as rest); (3) a well-balanced diet; (4) adequate and repeated explanation to allay fears; (5) avoidance of useless investigations; (6) extra care in treatment of lesions. Dr. Farquharson then discussed a few of the common conditions in old age—hypertension, obesity, strokes, Ménière's syndrome (often mistaken for a stroke)—and ended by pointing out that there was no need for specialists in geriatrics: "all that was needed was a sympathetic attitude of all doctors to their aging patients.

Dr. R. M. Janes, professor of surgery, University of Toronto, has been elected president of the Canadian Association of Clinical Surgeons, and of the Royal College of Physicians and Surgeons of Canada.

Branson Hospital is to be built by the Seventh-Day Adventists in North York at a cost of $1,400,000. Its capacity will be 100 beds.

The District meeting at Trenton heard these addresses: "Personal Investments for Medical Doctors" by Mr. R. A. Mitchell, research analyst of A. E. Ames and Company, Toronto; "Use and Abuse of Sex Hormones" by Dr. D. J. Van Wyck, clinical teacher, department of obstetrics and gynæcology, Toronto General Hospital; "The Rh Factor" by Dr. John Darte, research associate and clinical assistant, Hospital for Sick Children; "Fractures of the Wrist and Forearm" by Dr. F. P. Dewar, surgeon-in-chief of orthopædic surgery, Toronto General Hospital.

The Walkerton District meeting was addressed by Dr. Stewart Rogers, clinical teacher, Toronto General Hospital, on "Common Skin Diseases and Their Treatment," and by Dr. D. P. Murnaghan, clinical instructor, University of Toronto, on "Has the Patient Heart Disease?".

Dr. Frances Passcher, associate professor of dermatology, New York University Bellevue Medical Center, addressed the staff of Women's College Hospital on drug reactions. She deplored the promiscuous use of penicillin, suggesting other broad-spectrum antibiotics instead because of fewer reactions from them.

Skin manifestations after penicillin included discrete coin-shaped copper-coloured spots, scarlatiniform rashes, morbilliform rashes, generalized œdema of face, body, extremities and mucous membranes and localized mucous membrane reactions with exudate.

She mentioned the fact that LE cells had been found after the use of Apresoline but stated that cause and effect had not yet been made clear. The drug may have been a trigger in a patient who was developing the disease.

Dr. Joseph A. Sullivan was given an award by the American Academy of Otolaryngology at the recent Chicago meeting. This recognized his contributions to surgery of the inner ear, as well as the development of ear labyrinth studies carried on at St. Michael's Hospital, Toronto.

Dr. William Boyd was made an honorary fellow of the American College of Pathologists at the annual meeting held in Chicago. It was the third time in the history of the society that such an honour had been conferred. Other members to have been so honoured are Dr. George Whipple, Rochester, N.Y., who was awarded the Nobel prize for his work on pernicious anæmia, and Dr. Ludwig Hektoen, Chicago.

During the conferring of the honour Dr. Boyd was described as the world's foremost living writer on pathology, and an authority whose textbooks and treatises are accepted as standard reading in medical schools throughout the English-speaking world.

Dr. Boyd has recently been made an Honorary Fellow of the Royal College of Physicians of Edinburgh.

At present he is lecturing in the History of Medicine at the University of Toronto and goes for three months in the winter to be visiting professor at the University of Alabama.

LILLIAN A. CHASE

On June 20, 1955, to mark the 30th anniversary of the establishment of an intern service in the Department of Pathology, Hamilton General Hospital, the 75 past interns and residents organized and tendered to

four reports

attesting to the safety of

'Dexedrine' in

obese hypertensives

1

Goodman and Housel (the latter is chief of the Jefferson Hospital Hypertension Clinic, Philadelphia) conducted exhaustive studies of 100 obese hypertensives. They concluded:

- "Prolonged use of oral 'Dexedrine' does not affect the long term blood pressure in obese hypertensive patients."
- "'Dexedrine' consistently reduces the appetite. . ."

Goodman, E.L., and Housel, E.L.:
Am. J. M. Sc. 227:250 (March) 1954.

2

"There is no apparent effect on hypertension, and the drug can be used freely in hypertensives with obesity . . ."

Finch, J.W.: J. Oklahoma M.A. 40:119.

3

'Dexedrine' "has been given in cases where the blood pressure was over 200 systolic and 100 diastolic without any ill effects, and [many of] these patients have obtained . . . a drop in blood pressure."

Ferguson, H.E.: Virginia M. Monthly 76:222.

4

Livingston, after treating a series of 49 patients with 'Dexedrine' for 1-5 years reported that the blood pressure remained "essentially unchanged throughout the course of the treatment."

Livingston, S.; Kajdi, L., and Bridge, E.M.: J. Pediat. 32:490.

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Dr. William J. Deadman a banquet and presentation at the Estaminet Restaurant, Burlington, Ont. Contact had been made with 65 of the 75, and 45 with their ladies attended the banquet, including the first intern, Dr. R. C. Riley of Calgary, and others from as far afield as Bermuda, Hollywood, Cal., and Prince Rupert, B.C. Dr. A. J. Blanchard, pathologist at Sunnybrook Hospital, Toronto, acted as chairman. Dr. R. F. Hughes of Hamilton made a presentation of a beautiful pin to Mrs. Deadman. Dr. G. C. Kelly of Hamilton made a presentation of a wrist watch to Dr. Deadman. A toast to "the Chief" was proposed by Dr. H. A. Ansley of Ottawa, to which Dr. Deadman feelingly replied. Reminiscences of experiences in the laboratory over the 30 elapsed years were recounted by various members of the audience. Dr. Deadman has been Director of his Department for the past 36 years.

MEDAL FOR DR. BIGELOW

At a recent meeting of the International Society of Surgery Dr. W. G. Bigelow of Toronto was presented with the Society's medal. This is a new award which will be made every two years to some surgeon who has made a significant contribution to surgery. The 1955 medal is the first awarded, and its receipt by a Canadian is therefore a mark of special distinction. The International Society of Surgery is one of the oldest surgical societies in Europe and now includes members from all countries in Europe and from America. The President of the Society this year was Dr. Evarts Graham of St. Louis.

QUEBEC

OPENING OF THE NEW MONTREAL GENERAL HOSPITAL

Although it had been in operation for the last four months, the Montreal General Hospital held a special ceremony on October 4, when Her Royal Highness the Princess Royal formally declared the new buildings open; they were dedicated by the Lord Bishop of Montreal.

Princess Mary was received at the Hospital by the President, Colonel Stuart MacTier, and members of the medical staff who, with the Board of Management and selected guests, were presented. The ceremonies were held in Livingston Hall—the nurses' home—and were extremely colourful. In his introductory remarks the President of the Hospital referred to the visit to Montreal hospitals by the late King George V in 1896. It was peculiarly fitting that his daughter Princess Mary should officiate at this later stage in the life of the Hospital. He then presented Her Highness with a symbolic golden key of the Hospital inscribed with a presentation and the crest of the Hospital. With this symbol the Princess after a short address declared the Hospital open.

A tour of inspection of the Hospital was then made. the Princess showing the keenest interest in the patients and wards. More than once she asked to see additional parts of the buildings. In the maternity ward she showed her thoughtfulness in sending in to the mother of the latest born baby in the Hospital (a few hours old only) the bouquet with which she had been presented on entering the Hospital. The medical library of the Hospital also attracted her close attention, with its strikingly effective doorway brought up from the old buildings, and the various aphorisms and quotations inscribed on its walls. The tour ended with her signing the first page of the new visitors' register specially prepared for the Hospital by the consultant staff.

The new buildings need little to enhance their appearance both inside and out, but the brilliant autumn sunshine added a final touch of splendour to the impressive proceedings.

THE THIRD F. J. SHEPHERD LECTURE

The third Francis J. Shepherd Lecture was delivered in the Montreal General Hospital by Dr. E. P. Scarlett, Chancellor of the University of Alberta, on the afternoon of October 5. It was a most suitable opening event for the amphitheatre of the new building which with its excellent acoustics and well-arranged seating bids fair to be a popular place for future similar occasions.

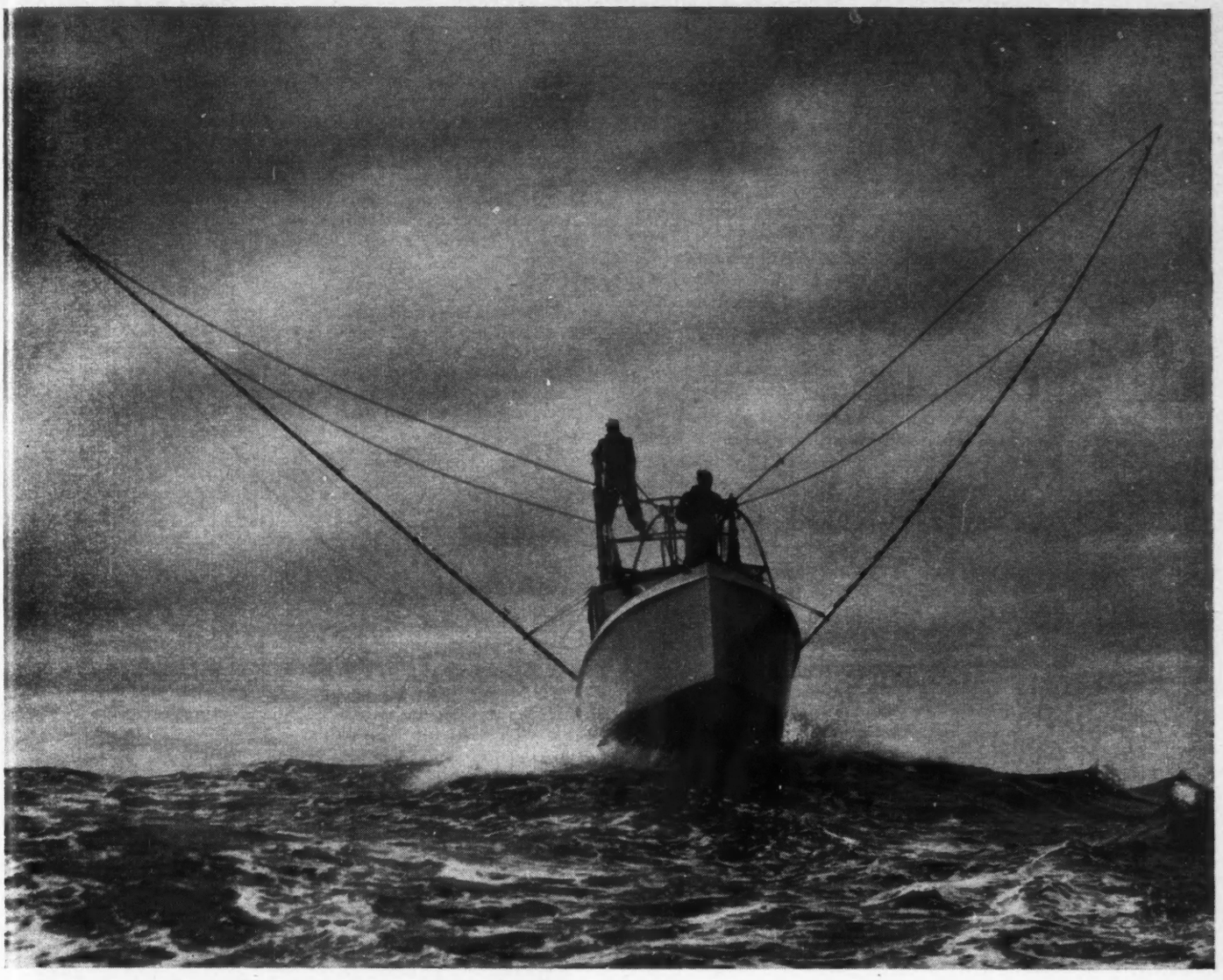
In introducing the speaker, Dr. H. E. MacDermot referred to Dr. Scarlett's variety of interests in the fields of medicine, history, music, and social and public work, and perhaps above all in education. It was fitting that he should give this lecture in honour of one who, himself widely cultured, had left an abiding mark in Canadian medical history.

Dr. Scarlett's address was a notable achievement in historical commentary. After his opening tribute to Dr. Shepherd and a fine soliloquy on the history of the hospital, he turned to the part played by men of its staff and graduates of the McGill medical school (for the two institutions were inextricably bound together) in the earlier days of medicine in Western Canada, a subject on which he was peculiarly qualified to speak. The earliest days of medicine in the West belong of course to the time of the trading companies, and the medical men who moved through the West at that time had not been trained in Canada; he merely sketched them in as a background. But from the early seventies onwards men of the Canadian schools of Montreal and Toronto began to turn west. Several went out to the Riel Rebellion campaign, notably Dr. (Sir) Thomas Roddick who was in charge of the medical arrangements and left an enviable record in a campaign which Shepherd described in his typically terse way as "a muddle". Dr. Scarlett managed to avoid mere listings of names, picking out unerringly those doctors who in some way or other made their mark—in medicine, in politics, or pioneering; Dr. Andrew Rutledge, for example, a McGill graduate who settled in Moosomin in 1883 and used to break in moose calves which he would hitch to a toboggan for the trails in winter; or F. H. Mewburn, "the little man with the powerful tongue", who has left the memory of a personality which one would be excused for calling "legendary" if it were not so fully attested. In later years of the period the list of names on the Faculty of Medicine of the University of Alberta read like a McGill roll of honour: Rankin in bacteriology and first Dean; Pope in medicine; Ower in pathology; Mewburn and Munroe in surgery; Conn and Harrison in obstetrics and gynæcology; Smith in urology. Amongst those in British Columbia were men like I. W. Powell whose name is commemorated in Powell Street in Vancouver, E. B. C. Hanington, R. E. McKechnie, who became Chancellor of the University of British Columbia, and Herman M. Robertson, who became president of the Canadian Medical Association.

These were only a very few of the men who, as Dr. Scarlett put it, wove the medical threads into the tapestry of the history of Western Canada.

At the conclusion of his address Dr. Scarlett was presented by Dr. Neil Feeney with the clock specially designed for this lecture by Professor Percy Nobbs, son-in-law of Dr. Shepherd.

There has been considerably increased activity in our Division in the last month or two, and the tempo of this activity will no doubt continue to climb, terminating in the 1956 C.M.A. Annual Meeting in Quebec City. A provocative tentative programme has been drawn up and submitted to the Central Committee by the Division's Programme Committee, chaired by Dr. H. S. Morton and including among its members Drs. Paul A. Poliquin and François Roy of Quebec, Dr. Murray R. Stalker of Ormstown, and Drs. Jacques Genest, Douglas G. Cameron,



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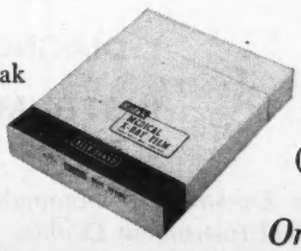

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Roger Dufresne, Edouard Gagnon, Alan S. Ross and A. H. Neufeld of Montreal.

An annual meeting like ours, particularly when taking place in a historical location such as Quebec City, entails a great deal of careful planning. Arrangements will be managed by a Committee consisting of Drs. D. S. Lewis, R. Vance Ward, W. deM. Scriver, and Léon Gérin-Lajoie of Montreal, Dr. Adélard Tétreault of Three Rivers, and Dr. T. James Quintin of Sherbrooke. Dr. Renaud Lemieux, assisted by Dr. C. A. Gauthier, will act in liaison with this Committee on General Arrangements. Drs. A. D. Kelly and Arthur Peart will be honorary secretaries, and Drs. Gerry Halpenny and Jacques Turcot of our Division will be the secretaries.

It would indeed be a great pleasure to name all those participating in the planning of our next year's annual meeting. However, since this would merely entail a long listing of names, only committees and their respective chairmen are given. Ceremonial Procedures and Entertainment will be chaired by Dr. Eustace Morin, assisted by Dr. Mathieu Samson of Quebec City. Finance will be under the guidance of Dr. J. G. Howlett of Montreal. Commercial exhibits are being arranged by Dr. Gustave Auger and his assistants, while scientific exhibits will be under the direction of Dr. Carleton Auger of Quebec.

Housing, a thankless and at times a painful problem, is being handled by Dr. Rosaire Gingras of Quebec and his associates. Signs and equipment are under the capable guidance of Dr. Samuel L. Pollack of Quebec and his committee. Information and registration will be handled by Dr. Marcel Langlois of Quebec and his committee, while transportation will be under the guidance of Dr. J. M. Elliott of Quebec and his group.

Founder's Day ceremonies at McGill University on October 6 were highlighted by the conferring of honorary degrees. Her Royal Highness, The Princess Royal, who was paying her first visit to Canada, received the honorary degree of Doctor of Laws. In addition, we were pleased to note that Dr. J. B. Collip and Professor E. G. D. Murray, former heads of the departments of biochemistry and endocrinology, and of bacteriology, respectively, each received the honorary degree of Doctor of Science.

The Association of French-speaking Doctors of Canada concluded a most successful 25th Annual Meeting in Montreal on Saturday, September 24. There was excellent national representation and both professional and business meetings were well attended. The decision was taken to hold the 26th Annual Meeting at Jasper, Alberta.

A. H. NEUFELD

NEW BRUNSWICK

Dr. John A. Finley has been appointed Associate Surgeon at the Saint John Tuberculosis Hospital.

Dr. John Stevenson, recently of Port Colborne, Ontario, has joined the staff of the Saint John General Hospital in the Department of Diagnostic Radiology.

The Saint John Medical Society honoured Dr. E. C. Menzies, one of its members, at a dinner at the Riverside Golf Club on September 27. Dr. Menzies recently retired from the position of Superintendent of the N.B. Provincial Hospital at Lancaster. In a speech characterized by his unusual type of humour, Dr. Menzies re-

viewed the history of the institution which he had served for 21 years. Dr. Menzies spoke of the difficulties met with by his four predecessors and wished success to his successor, Dr. Robert Gregory. The president of the Society, Dr. F. J. Cheesman, presented Dr. Menzies with a watch as an evidence of the regard in which he is held by his colleagues.

The appointment of Dr. Conrad Drolet as Medical Superintendent of the Provincial Hospital at Campbellton has been announced by the Honourable Dr. J. F. McInerney. Dr. Drolet has had excellent training in psychiatry and has been assistant psychiatrist at Saint Michael the Archangel Hospital, Quebec City.

Busy doctors seem to find time for civic duties. In Saint John this month Dr. J. P. McInerney has been appointed to the Board of School Trustees; Dr. George White has been elected President of St. George's Society, and Dr. Norman S. Skinner has assumed the duties of president of the Saint John Art Association.

On October 18, the Honourable Dr. J. F. McInerney, Minister of Health for New Brunswick, officially opened the new Red Cross Blood Depot in Lancaster. This new addition to the health services of the province is made available by the co-operation of the Canadian Red Cross Society and the Provincial Government. Speakers at this function included Lieutenant-Governor D. L. MacLaren; Mr. Vernon C. Hale of Hamilton, National Chairman of the Red Cross Blood Transfusion Service; Dr. George W. Miller of Toronto, National Director of the Service; and Dr. G. B. Peat, Mayor of Saint John.

Dr. Arnold Branch is the medical director of the service in the Saint John Depot.

Arising out of the annual meeting of the N.B. Medical Society held in September, the following decisions were made:

1. The choice of Blue Cross–Blue Shield as an indemnity plan in New Brunswick as adopted in 1951 was officially reapproved.

2. The action of the Society's executive in approving the Ford Company contract through Trans-Canada Medical Plans to be implemented by the local Blue Shield organization was confirmed. This approval applies also to other national contracts seeking the same type of coverage through T.C.M.P.

3. The C.M.A. Statement of Policy on Health Insurance, as of June 1955, was approved by the N.B. Division.

4. Medical Care of Welfare Group–the recommendations of the executive and economics committee were confirmed: (a) That no further action be taken by the Society to press the Government to establish a prepaid plan for the welfare group. (b) That the existing liaison between the Government and ourselves be continued.

A contribution to the Dalhousie Post-Graduate Programme of $1,131 for the fiscal year ending June 30, 1955, was approved.

A. S. KIRKLAND

CANADIAN ARMED FORCES

The Third Annual Conference of Senior Naval Medical Officers was held in the offices of the Medical Director General, Naval Headquarters, Ottawa, October 13 and 14, 1955. The conference, under the Chairmanship of Surgeon Commodore E. H. Lee, C.D., M.D., L.M.C.C., Q.H.P., Medical Director General, Royal Canadian Navy, was attended by Surgeon Captain T. B. McLean, C.D., M.D., L.M.C.C., Command Medical Officer, Pacific Coast; Acting Surgeon Captain F. G. W. MacHattie, C.D., M.D., D.P.H., L.M.C.C., Command Medical

Officer, Atlantic Coast; Surgeon Commander G. W. Chapman, C.D., M.D., L.M.C.C., Deputy Medical Director General, Naval Headquarters; Surgeon Commander W. J. Elliot, C.D., M.D., C.M., L.M.C.C., Principal Medical Officer, R.C.N. Hospital, Halifax, N.S.; Surgeon Commander J. W. Rogers, M.D., C.M., D.P.H., L.M.C.C., Principal Medical Officer, R.C.N. Hospital, Cornwallis, N.S.; Surgeon Commander J. H. Fleming, C.D., M.D., L.M.C.C., Principal Medical Officer, R.C.N. Hospital, Esquimalt, B.C.; Surgeon Lieutenant Commander W. C. Wood, M.D., C.M., L.M.C.C., Staff Medical Officer to the Flag Officer Naval Divisions, Hamilton, Ont.; and Lieutenant Commander (MAd) S. T. Richards, C.D., Assistant Medical Director General (Plans), Naval Headquarters. The Secretary to the Conference was Lieutenant (MAd) V. H. Skinner, C.D., R.C.N.

It is with regret that we report the death of Surgeon Lieutenant Commander Robert E. Stewart, M.D., R.C.N., on September 19, 1955. Dr. Stewart, who was 33, was taking postgraduate training in internal medicine at St. Michael's Hospital, Toronto, at the time of his death. The funeral took place at St. Aidan's Anglican Church, Toronto, with full naval honours. Interment was in Resthaven Cemetery, Toronto.

An outbreak of poliomyelitis occurred at No. 1 Fighter Wing (R.C.A.F.), Marville, during the latter half of August and the first week in September. There was a total of 26 cases, including 12 cases with paralysis. Concurrently there was a sharp increase in the incidence of the disease in the local civilian population in France and in Belgium. Dr. Milton H. Brown, Consultant Physician in Preventive Medicine to the Canadian Forces Medical Council, accompanied by W/C W. W. Laughland, R.C.A.F., D.G.M.S. (Air) Branch, visited the Air Division Wings in France to investigate the epidemiology of the outbreak.

A Conference of Commanding Officers, R.C.A.F. Auxiliary Medical Units, was held at the Institute of Aviation Medicine, Toronto, on October 28 and 29 under the chairmanship of Air Commodore A. A. G. Corbet, Director General of Medical Services (Air).

Lieutenant-Colonel V. Radoux, R.C.A.M.C., is undertaking a course in hospital administration at the University of Toronto.

Major J. A. Lewin, R.C.A.M.C., and Captain P. Perron, R.C.A.M.C., commenced senior internships in internal medicine last July at Lancaster Hospital, D.V.A., Saint John, N.B.

Captain S. W. Potter, R.C.A.M.C., began a senior internship in obstetrics and gynæcology, and Captain J. R. McIver, R.C.A.M.C., a senior rotating internship, at the Ottawa Civic Hospital, Ottawa, last July.